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RECLASSIFICATION OF THE ANEMIAS

REUBEN OTTENBERG, M.D.

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In the last ten years a revolution has occurred in the views of anemia. To indicate what the advance has been I propose (1) to review briefly the work of a series of experimenters and clinicians, (2) to present a new classification of the anemias based on their work, and (3) to discuss the methods of therapy.

REVIEW OF RECENT RESEARCH

The ball was set rolling, so to speak, by an extraordinary series of researches planned on a large scale, begun before 1920 and continued with great industry to the present day by Whipple and Robscheit-Robbins [1] at the University of Rochester, N. Y. These workers studied the treatment of long sustained secondary anemia in the dog by various diets and other forms of therapy. They cleared up many inconsistencies in the work of their predecessors by the manner in which they brought about the anemias in the dog. It would take me too far afield to describe their technic in detail, but the essential point is this: After a single hemorrhage or a few repeated hemorrhages or after an acute destruction of blood, the body still retains a large store of potential blood-forming material. It requires three or four months of persistent bleeding and a diet containing a minimal and known amount of such blood-making material (namely, a diet of a special bread) to use up this potential store. By careful hemoglobin determination, blood volume estimations, and the like, it is possible to estimate with great exactness how much hemoglobin the dog is capable of manufacturing per week.

Dogs that have thus been gradually brought to the base line and kept on the special bread diet (which is adequate in every other way to maintain their health) produce about 3 Gm. of hemoglobin in a standard two week period. When other foods or medications are added to the standard bread diet, their effect on blood formation can readily be learned. Table 1 presents a selection of the most significant of a large number of substances investigated by Whipple and Robscheit-Robbins; it shows how much hemoglobin the addition of each of these substances to the diet enables the dog to make in the two week period.

For dogs, at least, the green vegetables fall far short of their reputation. Spinach produces only 15 Gm. of hemoglobin in two weeks. This may well be, of course, because the dog is a carnivorous animal. It is quite certain that the Herbivora oxen, for example, can utilize chlorophyll in blood formation; it is probable from clinical observation that man also can to a certain extent. However, it is not merely the vegetable origin of the material that is important. Many of the fruits in the table, such as peaches and apricots, lead to as much blood formation in the dog as do the best varieties of animal foods, with the exception of kidneys and liver. It is interesting to note that beef, in spite of its reputation as a blood maker, stands only a little above the green vegetables. The most important fact discovered by Whipple and Robscheit-Robbins was the enormously stimulating effect of a diet containing large amounts of mammalian kidney and, above all, of a diet containing adequate amounts of mammalian liver. Surprisingly enough, fish liver has no more potency than fish itself. Beef liver leads to an average production of 95 Gm. of hemoglobin in two weeks. These authors confirm the well known stimulating effect of inorganic iron in secondary anemias; in suitable doses it leads to the production of 55 Gm. of hemoglobin in a two week period. The iron normally present in the liver is evidently not the only factor in the effectiveness of liver as a blood producer, since optimal doses of iron produce less hemoglobin than does liver itself. An enormous amount of hemoglobin is produced by the combination of liver with inorganic iron; namely, 140 Gm. in the two week period. As Whipple and Robscheit-Robbins point out, no inorganic factor (even the combination of iron and copper to be referred to later) can compare to a suitable diet in this form of anemia.

The second great series of researches are those of Minot and Murphy [2] and a large group of active workers that has grown up around them at Harvard University. Their first important announcement was made in 1926. Stimulated by Whipple's work, Minot and Murphy tried in a systematic way a great variety of different diets in all sorts of clinical anemias. At first they came to the conclusion that a diet rich in animal protein was favorable for anemia. One cannot but admire the courage and thoroughness with which they insisted on carrying this out, thereby making their important discovery. Other clinicians, aware of Whipple and Robbins' work, had tried adding some liver and kidney to the diet of anemia cases and had casually observed good results. Minot and Murphy were, however, not satisfied with trying small amounts taken irregularly, but made their patients consume from one-half to 1 pound of liver a day.

Time will not permit me to go into the details of the effects of liver in pernicious anemia cases; so much has been written and said on the subject in the last few years that the facts are common knowledge. I may say

From the Medical Service, Mount Sinai Hospital.

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1. Robscheit-Robbins, F. S.: Physiol. Rev. **9**: 688 (Oct.) 1929.

2. Minot, G. R., and Murphy, W. P.: Treatment of Pernicious Anemia by a Special Diet, J. A. M. A. **87**: 470 (Aug. 14) 1926; A Diet Rich in Liver in the Treatment of Pernicious Anemia, ibid. **89**: 759 (Sept. 3) 1927.

briefly that with an adequate amount of liver or liver extract (in a subsequent section I will discuss what is meant by "adequate") the first effect is the increase in appetite and sense of well being and an increase in the number of reticulated red blood cells in the circulation from less than 1 per cent to 5, 10 or even 20 per cent in from five to seven days. This outpouring of young reticulated red blood cells from the bone marrow is temporary and is succeeded in the following weeks by a progressive increase in the hemoglobin and the number of red blood cells. The rise in the red blood cells in patients who are quite anemic (namely, have 2½ million or less to start with) is more rapid than that of the hemoglobin, so that the color index soon becomes normal. It is not unusual to observe an increase of from 1 to 3 million red blood cells in the first three weeks, and at the end of four months they are usually normal in number. The white blood cells begin to increase at the same time as the reticulocytes; the blood platelets, which are also depressed in pernicious anemia, begin to increase somewhat later. Within a few weeks there is a sharp increase in the percentage of eosinophilic leukocytes, sometimes to more than 20 per cent, if whole liver is taken. This persists for many weeks and then gradually returns to normal. The evidences of excessive blood destruction, such as the yellow color of the patient and the elevated icterus index in the blood serum, disappear in a few weeks. The atrophy of the tongue and the other tongue symptoms usually disappear by the time the blood has become normal. Neurologic symptoms, however, improve to only a limited extent, if at all. But in cases in which the blood can be brought to normal and kept normal, there is generally no further progression of the neurologic symptoms already present.

TABLE 1.—*Average Hemoglobin Production of Anemic Dogs in a Two Week Period as Influenced by Diet* *

Diet	Hemoglobin, Gm.
Bread alone	3
Bread and milk	3
Bread and spinach	15
Bread and apricots	48
Bread and eggs	45
Bread and whole fish	13
Bread and beef	17
Bread and kidney	70
Bread and beef liver	95
Bread and liver extract No. 343	10—20
Bread and iron	60
Bread and beef liver and iron	140

* Whipple and Robscheit-Robbins.

How does the liver diet work? Before 1926, approach to the problem of pernicious anemia was based on the conception of a hemolytic toxin. It is hard to believe that the liver diet merely stops a hemolytic process, although undoubtedly it does that also. Peabody, in 1927, began making biopsies on the bone marrow of patients undergoing liver treatment. He observed that the liver stimulates the maturation of the immature cells that crowd the marrow, and he noted the decrease of the megaloblasts in the marrow as the patient improved. This probably answers the old search for a hemolytic toxin in cases of pernicious anemia, referred to again and again in the older literature. Probably there is no toxin, but the cells disintegrate more rapidly than normal cells because they are turned out in an immature condition. What the specific substance in the liver does is to supply the patient with a sufficient amount of something that his body has lacked for a long time that is necessary for the complete maturation of red blood cells.

Incidentally, the simple clinical procedure of making bone marrow biopsies, introduced by Zadek, is becoming one of increasing value in understanding and diagnosing various blood conditions.

The next important step was the investigation into the nature of the substance present in liver which produces these extraordinary effects in pernicious anemia. This work, done particularly by Edwin Cohn and a group of other investigators associated with Minot,[3] has proceeded step by step in a systematic and difficult course and has resulted in the concentrated liver extracts that are now available to every practitioner for use by mouth or by injection. It has become apparent that in pernicious anemia what effects the cure is only a minute part of the 250 to 500 Gm. of crude liver which the patient needs each day. As little as 0.6 Gm. (10 grains) a day of Cohn's purest fraction is enough to produce a pronounced response in pernicious anemia cases. The active principle is easily soluble in water but is precipitated by alcohol or ether. It is free of iron as well as of protein, carbohydrate and lipoid and is apparently a nitrogenous base or polypeptide. Its precise chemical composition is not yet unearthed, as the pure substance has not yet been isolated.

The next great advance in knowledge of the nature of pernicious anemia came from Castle and a group of his associates in Boston who worked independently of Minot. In order to appreciate this work it is necessary to go back some years and refer to the gradual recognition of the central rôle which the absence of hydrochloric acid from the stomach plays in pernicious anemia. The occurrence of this phenomenon was discovered independently by von Noorden in 1891 and by Einhorn in 1892, but it was Kurt Faber,[4] in 1900, who first studied a large series of cases and showed that the achlorhydria is an essential part of the disease. In subsequent studies, Meulengracht in Scandinavia and Hurst in England (1923) showed not only that the absence of acid is characteristic of the disease but also that it regularly precedes all other symptoms of the disease and does so by years. Not one case of pernicious anemia has been reported which, examined prior to the disease, had a normal functioning gastric mucosa. Furthermore, it was shown that the achylia, once established, is permanent and that it occurs with undue frequency in the families of patients with pernicious anemia. It is now believed that the tendency to develop achlorhydria in middle age is the constitutional basis that predisposes to the development of pernicious anemia.[5]

Knowing this, Castle[6] set to work to investigate the relation of the stomach to the production of the antianemic principle that is curative in pernicious anemia. He quickly found that the administration of hydrochloric acid, of pepsin or of normal gastric juice to pernicious anemia patients was without effect. But if chopped meat was first thoroughly digested with gastric juice and then administered to pernicious anemia patients by stomach tube the result was phenomenal. It was equivalent to the administration of liver extract itself. The gastric juice of pernicious anemia patients incubated with meat is entirely without effect even if pepsin and hydrochloric acid are added, so that normal digestion proceeds.

3. Cohn, E. J.; Minot, G. R.; Alles, G. A., and Salter, W. T.: J. Biol. Chem. **77**: 325 (May) 1928.
4. Faber and Bloch: Ztschr. f. klin. Med. **40**: 98, 1900.
5. Cornell, B. S.: Medicine **8**: 398 (Sept.) 1927.
6. Castle and Locke: J. Clin. Investigation **6**: 2, 1928. Castle, W. B.; Townsend, W. C., and Heath, C. W., ibid. **9**: 2 (Aug.) 1930. Castle, W. B.: Am. J. M. Sc. **178**: 748-764 (Dec.) 1929. Castle, W. B.; Heath, C. W., and Strauss, M. B.: ibid. **182**: 741 (Dec.) 1931. Strauss, M. B., and Castle, W. B.: New England J. Med. **207**: 55 (July 14) 1932.

It is evident that there is some essential substance present in normal gastric contents, called by Castle the "intrinsic factor," and another essential substance present in beef muscle and certain other foods, called by him the "extrinsic factor." The interaction of these two substances under conditions that are favorable to the digestion of proteins produces in the stomach the antianemic principle which is curative in pernicious anemia. Apparently the antianemic principle so formed is absorbed and stored in the liver, which thus becomes the chief source for obtaining it.

The intrinsic factor in normal gastric juice is neither hydrochloric acid nor any of the usual enzymes; nor is it the antianemic substance itself, as is seen from the following observations:

1. The gastric juice alone does not produce the curative effect.

2. The intrinsic substance in gastric juice is thermolabile, being destroyed at 70 C. in half an hour, or by 40 C. in three days, while the antianemic substance is thermostable, resisting cooking and boiling for a reasonable length of time.

3. The intrinsic factor acts on beef muscle even at a neutral reaction, while pepsin reacts only in an acid reaction.

4. Gastric juice freed from pepsin and rennin by absorption methods still is effective on beef muscle.

The extrinsic factor is present not only in beef muscle but in a number of other substances, including yeast. It is absent, however, from many proteins such as casein, wheat glutein and nucleoprotein and is also absent from nucleic acids derived from animal sources and from yeast. There are some reasons for believing that it is related to vitamin B_2 or G (active in pellagra).

Pursuing this line of thought, Sturgis and Isaacs [7] at Ann Arbor, Mich., have introduced a practical and useful addition to the therapeutic armamentarium; namely, desiccated hog stomach. They found that the whole stomach of the hog, freed of extraneous substances including fat, chopped up fine and dried without the aid of too much heat, was equivalent in value to liver extract and had practical advantages over liver extract in certain cases. A knowledge of Castle's observations explains why it was that Sturgis and Isaacs found that neither the mucous membrane of the hog's stomach nor the muscular layer alone was effective, but that it was necessary to administer the two together in order to obtain the antianemic effect. The mucosa provides the intrinsic substance; the muscular layer, the extrinsic substance.

Clinical experience has shown that liver extract is potent not only in pernicious anemia but also in sprue and certain other related anemias; but in spite of its enormous potency in these anemias it is entirely inert in anemias secondary to hemorrhage and to a large group of other causes. This apparent contradiction of the fundamental animal observations of Whipple and Robscheit-Robbins on the effect of liver diet in secondary anemia led them to compare the effect on secondary anemia not only of liver extract (No. 343), as used in pernicious anemia, but of numerous other liver fractions prepared in different ways. They found that the effect of the liver extract was trifling, only 20 Gm. of hemoglobin being produced in two weeks as compared with 95 Gm. produced by the feeding of whole liver, and 140 Gm. produced by the feeding of liver and inorganic iron. In fact, it turned out that there were many other fractions in liver, including especially certain mineral substances present in the ash, which have a more marked stimulating effect in the production of red blood cells in this variety of anemia. The effect of the antianemic substance of Minot and Cohn can be demonstrated only in human cases that have an actual deficiency of it, as pernicious anemia.

The meaning of Whipple and Robbins' observations will be clearer after a discussion of the important results that have come in recent years from the studies of the nutritional anemias of the rat. If young rats are fed an exclusive milk diet, they develop an extreme grade of anemia comparable in many ways to the nutritional anemias of infants. Recently it has been shown that exactly the same occurs with suckling pigs and other mammals. A large number of workers in different localities have studied the effect of various therapeutic procedures on this nutritional anemia of rats.

The most important result has been that of Steenbock, Hart and their group of workers.[8] They found that this anemia is not cured by chemically pure iron alone but that the addition to iron of the ash of various plants causes a complete cure. Fractionation, that is to say, the addition to iron of each chemical ingredient of the ash, showed that apparently copper is the missing link without which iron is relatively ineffective. An exceedingly small trace of copper is all that is needed; this is why the importance of copper had been overlooked before. If the iron is not especially purified, for example, or if the milk that is fed the animals is collected in copper lined pails, the animals receive enough copper to supplement the iron.

For this reason, there is some doubt still about the need for therapeutic administration of copper with iron. Certainly it is important to remember that an extremely small amount of copper is all that is needed and that too large a dose of it may have toxic effects. The work of some authors suggests that copper is not alone in its ability to supplement iron but that manganese, cobalt and other elements may have at least some of the same effect. This is denied by Hart and his school, who believe that the other investigators do not sufficiently purify their food of copper. The question of the value of other elements is at present a matter of controversy. However, it is conceded by all that a small amount of copper, itself inert, when added to chemically very pure iron, which alone is relatively inert, confers on the iron enormous potency in the nutritional anemia of young mammals.

Clinicians for years have been familiar with the fact that iron was effective in anemia due to blood loss, whereas in anemia due to destruction of blood in the body (hemolysis) iron had relatively little effect. It was shown by Muir [9] and many others that when hemolysis occurs in the body practically all the iron from the disintegrated red blood cells is conserved in the body, chiefly in the liver. It is apparent then that one of the chief ways in which iron administration does its work in anemia due to blood loss is by supplying that absolutely essential building stone, the iron atom at the center of the hemoglobin molecule. While in order to get a therapeutic result it is necessary to give very large doses of iron, only a small amount of the iron admin-

7. Sturgis, C. C., and Isaacs, Raphael: Desiccated Stomach in the Treatment of Pernicious Anemia, J. A. M. A. **93**: 747 (Sept. 7) 1929. Sharp, E. A.: An Antianemic Factor in Desiccated Stomach, ibid.: **93**: 749 (Sept. 7) 1929.

8. Hart, E. B.; Steenbock, Harry; Waddell, J., and Elvehjem, C. A.: J. Biol. Chem. **77**: 797 (May) 1928. Waddell, J.; Steenbock, Harry, and Hart, E. B.: ibid. **83**: 243 (July) 1929; **84**: 115 (Oct.) 1929. Elvehjem, C. A., and Hart, E. B.: ibid. **95**: 363 (Feb.) 1932.

9. Muir and Dunn: J. Path. & Bact. **19**: 417, 1914-1915.

istered by mouth is absorbed. But that part absorbed is almost quantitatively converted into hemoglobin.[10] In suitable cases, iron appears to stimulate the bone marrow in very much the same way as liver extract does in pernicious anemia. There is first an outpouring of young red cells (reticulocytes),[11] and this is followed by a gradual increase in hemoglobin and red blood cells. However, in the case of iron the hemoglobin is produced more quickly than the red blood cells, tending to bring the low color index up to normal, whereas with liver extract the production of red blood cells is more rapid than that of hemoglobin, tending to bring the high color index down to normal.

It is evident then that both iron and liver extract act by supplying a deficiency. In line with this conception of the action of iron is the fact, observed by Robscheit-Robbins and Whipple, that there is an optimal dose of iron, and that when this dose has been reached and the maximal amount of hemoglobin that can be produced by iron (for dogs, from 50 to 60 mg. of hemoglobin in a two week period) has been attained, a further increase of the dose of iron does not lead to more rapid increase in hemoglobin. However, the addition of liver or kidney to this optimal dose of iron leads to a much greater increase in hemoglobin; namely, 140 Gm. in two weeks. It is evident then that in secondary anemia there are at least two substances which need to be supplied (and undoubtedly there are many more than two) the one iron, the other, whatever it is, that the whole liver supplies.

A NEW CLASSIFICATION

In view of these important investigations and of a large number of parallel clinical studies, only a few of which can be briefly referred to here, it is evident that a new classification of clinical anemias based on present improved knowledge of blood regeneration is needed. The older classifications, such as those of Ehrlich, Hirschfeld, Pappenheimer and Naegeli, were based chiefly on morphology and to some extent on etiology; they separated the group of "primary" anemias because their causes were unknown. The present attempt at classification is based essentially on pathogenesis, so far as discovered, and is correlated with the effects of therapy.

The classification that I present in table 2 is divided into three broad divisions: (1) deficiencies, (2) direct injury to the blood-making organs, (3) blood destruction from whatever cause. There is no fundamental division into primary and secondary anemias, because there are no primary anemias. Every anemia has a cause, although in some cases the cause is still unknown, and the anemia can be classified only on its apparent pathogenesis.

This classification, made necessary by advancing knowledge, is, of course, in itself only a temporary one. It will no doubt have to be revised as soon as new information is at hand. Also, since anemia is a symptom, never a disease, this is not so much a classification of diseases as of anemias due to different mechanisms occurring in different diseases.

In many instances a given condition may have to be classified under two headings. For example, some cases of Bothriocephalus anemia have a group relationship to pernicious anemia and respond to liver therapy; others present only the picture of a hypochromic anemia, and recovery occurs after the removal of the worms. The same thing is true of pregnancy anemia: some patients do well on liver therapy while others require only iron. In many of the hemolytic anemias there is a possibility that some element of injury to bone marrow may play a rôle. Conversely, it is probable that in some of the group in which the injury to the hematopoietic organs is the predominating mechanism some degree of hemolysis may occur.

In some cases, as for example certain infantile anemias classified under nutritional deficiencies, the assignment of the condition is a mere guess, since the true

TABLE 2.—*New Classification of Anemias*

I. DEFICIENCIES

A. IRON DEFICIENCIES
1. Blood loss
   (*a*) Acute
   (*b*) Chronic
   (*c*) Hookworm anemia
2. Hypochromic anemia
   (*a*) Chlorosis
   (*b*) Simple hypochromic anemia
   (*c*) Achlorhydric anemia
   (*d*) Hypochromic anemia of pregnancy
3. Simple nutritional anemia of infants (on exclusive milk diet)
   (*a*) Anemia of premature infants

B. DEFICIENCY OF "ANTIANEMIC PRINCIPLE"
1. Pernicious anemia
2. Sprue
3. "Pregnancy pernicious anemia"
4. Bothriocephalus anemia (certain cases)

C. NUTRITIONAL DEFICIENCIES
1. Avitaminoses—anemia of beriberi, pellagra, scurvy, rickets
2. Loss of bile or of pancreatic secretion
   (*a*) Bile fistula anemia
   (*b*) Pancreatic or duodenal fistula
3. Failure of intestinal absorption
   (*a*) Chronic diarrheas, sprue (some cases), celiac disease
   (*b*) Small intestinal stenosis
4. Nutritonal anemia of adults
5. Certain infantile anemias (von Jaksch, Cooley)

II. INJURY TO THE BLOOD-MAKING ORGANS
(Interference with blood regeneration)

A. TOXIC DESTRUCTION OF MARROW
1. Aplastic anemia secondary to:
   (*a*) X-rays, radium, thorium
   (*b*) Benzene, arsphenamine, nitrobenzene, trinitrotoluene
   (*c*) Lead, mercury, etc.
2. "Primary" aplastic anemia (toxic agent not yet known)

B. MECHANICAL REPLACEMENT OF MARROW
1. Osteosclerosis
   (*a*) Osteosclerotic anemia
   (*b*) Marble bone disease (Albers-Schönberg)
2. Gaucher's and other lipoid deposits in marrow (Niemann-Pick, Schuller-Christian)
3. Leukemia and Hodgkin's disease } (Toxic factor also)
4. Metastatic new growths in marrow }

C. INTERFERENCE WITH BLOOD REGENERATION AT SOME INTERMEDIATE STAGE
1. Diseases of the spleen
   (*a*) Banti syndrome ("splenic anemia")
   (*b*) Sclerosis or thrombosis of splenic vein
2. Diseases of the liver
   (*a*) Cirrhosis
   (*b*) Prolonged obstructive jaundice

III. DISINTEGRATION OF BLOOD (hemolysis)

A. CAUSED BY HEREDITARY DEFECTS OF RED BLOOD CELLS THEMSELVES
1. Hemolytic icterus
2. Sickle cell anemia

B. TOXIC DESTRUCTION OF BLOOD
1. Infections
   (*a*) Bacteria—all varieties, especially those invading the blood: hemolytic streptococcus, Staphylococcus aureus, Streptococcus viridans (bacterial endocarditis)
   (*b*) Protozoa—malaria, kala-azar, syphilis
   (*c*) Acute febrile hemolytic anemia (cause unknown)
2. Intestinal Worms—Bothriocephalus
3. Cancer (including leukemia and allied diseases)
4. Nephritis—azotemia
5. Extensive burns
6. Hemolytic poisons
   (*a*) Serum hemolysins: { paroxysmal hemoglobinuria / incompatible transfusion
   (*b*) Chemical: { saponin, pyrodine, tolylenediamine, pyrogallol, snake venom, mushroom poison, phenylhydrazine, potassium chlorate

10. Heath, C. W.; Strauss, M. B., and Castle, W. B.: J. Clin. Investigation **11**: 1293 (Nov.) 1932.
11. Weiss, M. A.: Folia haemat. **33**: 57 (Sept.) 1926.

mechanism of the anemia is not yet certain; in these instances, the present scheme may at least serve as a convenient framework and perhaps lead to clearer thinking.

The classification is for the most part self explanatory, and it is unnecessary in the present article to discuss all its headings. A few points of special interest will be taken up in order.

That continued anemia due to simple blood loss is essentially an iron deficiency is now well recognized. Loss of blood in a single instance, if not too large, is rapidly regenerated without any specific iron medication, for the reason that the body contains within itself a considerable reserve store of iron. In prolonged or repeated blood loss, iron medication is usually needed because the reserve stores are used up. The contrast between chronic blood loss producing iron deficiency and a hemolytic type of anemia (in which the blood is destroyed in the body and the iron derived from the hemoglobin is almost entirely conserved in the spleen and liver) is brought out beautifully by the studies of Rhodes [12] on hookworm and other anemias in Puerto Rico. He found that iron alone, even with a poor diet and without the parasites being removed, will cure the anemia and keep the patient well; but if the parasites are removed and the iron is not given, it takes a year or more for blood regeneration to occur. On the other hand, in cases of malaria with an equal degree of anemia, it is not necessary to give iron; quinine alone is needed in order to kill the parasites, after which recovery from the anemia occurs spontaneously.

The second heading under iron deficiency, namely, hypochromic anemias, includes a group of important and common diseases whose mechanism is only just beginning to be understood. There is considerable doubt at present whether they represent separate diseases or a single syndrome. The one thing in common in this group of anemias, however, is that they are all promptly cured by adequate doses of iron. About chlorosis, which used to be regarded as a very common disease and which now is rarely seen in its so-called pure form, there has been a great deal of controversy. Naegeli and a group of older clinicians insist that there is such a disease as chlorosis and that it is an entirely separate entity and is easily diagnosed by a combination of rather rigid characteristics: (1) exclusive occurrence in females, (2) commencement at puberty, (3) absence of external causes of anemia, (4) absence of toxic symptoms, (5) characteristic blood picture, and (6) characteristic response to iron.

On the other hand, recent writers, such as Bloomfield [13] of Stanford University School of Medicine, deny that chlorosis is an entity at all. They point out that it grades off indistinguishably into the general group of chronic hypochromic anemias: that so-called chlorosis is not limited to the female sex, since cases identical in every regard, excepting sex, occur in males. (Witts, for example, who nevertheless regards chlorosis as a separate entity, describes sixteen cases, eight of them in males.) The occurrence of normal gastric acidity likewise is no definite distinction. While it is true that most of the younger individuals with chronic hypochromic anemia have normal gastric acidity and about 90 per cent of the middle aged and older patients have achlorhydria, there still remain about 10 per cent of the latter patients who have a normal gastric acidity.

12. Rhodes: Proc. Soc. Clin. Investigation, May, 1932.
13. Bloomfield, A. L.: Relations Between Primary Hypochromic Anemia and Chlorosis, Arch. Int. Med. **50**: 328 (Aug.) 1932.

The one characteristic common to the group of hypochromic anemias in middle aged and older persons (simple hypochromic anemia without achlorhydria and achlorhydric anemia) is the regular therapeutic response through no other treatment than iron. Belonging to the female sex or having deficient acid in the stomach are very strong predisposing factors, but the disease, nevertheless, can occur without one or both of these factors. It may be that the reason for the predominance of the female sex is merely the repeated though slight blood loss at menstruation; as tending to confirm this, in many of the cases in males there is a history of occasional blood loss from bleeding hemorrhoids, peptic ulcer or some other cause. The relationship of anacidity to this group of anemias is understood from the observation of Mettier and Minot [14] that the best absorption of iron from the upper portion of the intestine occurs when the contents of the duodenum are somewhat acid. Nevertheless, it is important to note, as was proved by Witts,[15] that the administration of hydrochloric acid aids blood regeneration only on iron therapy and then only if the dose of iron given is inadequate. The administration of hydrochloric acid is not necessary if the dose of iron is sufficient. It seems convenient, at least tentatively, to separate those cases of hypochromic anemia which have normal or only slightly diminished gastric acidity from those cases which have total achlorhydria and to keep the term "chlorosis" for the occasional cases which fulfil all the requirements of the classic description. The term "chloranemia," however, should be dropped as merely confusing.

Pregnancy anemia is one of the subjects about which there has been a great deal of confusion. Possibly this confusion is due to the fact that, even when the cases included in this term are strictly limited to those not due to complications but resulting from the gravid state itself, the anemia in different cases may be due to different causes. Larrabee,[16] in 1925, pointed out that there are two types of cases. The first, the so-called secondary type or hypochromic anemia of pregnancy, while it may be very severe, frequently responds rather well to iron treatment. Further experience, particularly that of Strauss,[17] has shown that some of these cases present a complete achylia and in all likelihood belong in the group of simple achlorhydric anemias just discussed. The other type of pregnancy anemia, the so-called pernicious anemia type, will be discussed under a later heading.

Anemias of infancy and the peculiar anemia of premature infants form another group about the pathogenesis of which there has been a great deal of confusion. Undoubtedly they do not represent a pathogenic entity. However, especially from the recent work of Helen Mackay [18] in London, it is clear that there is a very common form of simple anemia in infants analogous to the experimental anemia produced in animals by Bunge many years ago; this form of anemia responds specifically to iron therapy and is therefore most properly classed as an iron deficiency. From the work of Mackay it is also probable that the anemia which regularly appears in premature infants is due to the same cause but occurs with greater regularity and severity because the iron reserves at birth are smaller.

14. Mettier, S. R., and Minot, G. R.: Am. J. M. Sc. **181**: 25 (Jan.) 1931.
15. Witts, L. J.: Proc. Roy. Soc. Med. **24**: 543 (March) 1931.
16. Larrabee, R. C.: Severe Anemias of Pregnancy and Puerperium, Am. J. M. Sc. **170**: 371 (Sept.) 1925.
17. Strauss, M. B., and Castle, W. B.: Lancet **1**: 1198 (June 4) 1932.
18. Mackay, Helen M. M.: Anemia in Infancy, Arch. dis. Childhood **3**: 132 (June) 1928.

The anemia of premature infants also responds to adequate doses of iron. The method of its administration will be discussed later under the heading of iron therapy. Certain other peculiarities of infantile anemias will be discussed under the heading of nutritional deficiencies.

The next general group of deficiency diseases, those due to the deficiency of the "antianemic principle" of Minot, is the group which more than any other has caused recent revision of ideas of the pathogenesis and the classification of anemias. About pernicious anemia itself I shall say nothing at present. I have already discussed certain important features, and so much has been said about it in the last few years that it is an old story.

Close relationship of sprue and pernicious anemia has been suspected for a number of years on purely clinical grounds. Wood [19] showed as long ago as 1919 that in regions in which sprue is common there are many cases which one could with equal plausibility call sprue or pernicious anemia. It is true, however, that in about one half of the cases of sprue some hydrochloric acid occurs in the stomach, and that in a great many of the cases the blood picture is that of the hypochromic rather than of the hyperchromic type of anemia. While before the discovery of liver diet some patients with sprue recovered on certain dietetic treatments, it is now known that the great majority recover on treatment with liver diet or liver extract alone. A few cases are refractory and in some of these recovery takes place when liver extract is given intravenously. A few patients recover only when iron is added to liver. As some patients recover on dietetic measures alone, Castle suggests that in sprue there may be either deficiency of the intrinsic factor (as in pernicious anemia) or of the extrinsic (dietetic) factor. The latter probably are the patients who recover on dietary measures without the addition of the antianemic principle. Finally, in addition to either or both of these factors, he suggests that improper intestinal absorption may play a rôle in some cases and that these are the cases in which recovery occurs only when liver extract is used intramuscularly.

The third form of anemia in which the deficiency of the antianemic principle sometimes plays a rôle is the so-called pernicious anemia of pregnancy. As was pointed out previously, certain cases of pregnancy anemia, and usually the severest cases, present a blood picture closely resembling that of pernicious anemia. These cases may or may not present achlorhydria, but Evans,[20] Peterson,[21] Strauss [22] and others have shown that even patients who have hydrochloric acid in the stomach juice may be suffering from a lack of the antianemic principle and may get well promptly on the administration of liver extract.

Lucy Wills [23] has shown in India, where pregnancy anemia is very common and very fatal, that it can be cured not only by liver extract but also in many cases by yeast extract. As both liver and yeast extract contain large amounts of vitamin B_2 (known also as G and discovered first in connection with pellagra), she believes that it is the vitamin content which is important in this type of pregnancy anemia. In a certain number of cases of pregnancy anemia recovery also occurs, as was shown by Larabee, with persistent transfusion. Whether the transfusions are effective because they supply the necessary vitamin is not certain. There is no doubt, though, that with all these newer methods of treatment at one's disposal the prognosis of this disease (which was said by Minot in 1916 to have a mortality of over 60 per cent) is very much better than formerly.

One difference between the so-called pernicious anemia of pregnancy and true pernicious anemia is that in the former, if the patient recovers after the pregnancy, she remains entirely well without continuance of treatment, although the anemia may recur in subsequent pregnancies.

Most of what was said about sprue and pernicious anemia of pregnancy is also true of Bothriocephalus anemia. It has been known for years that only certain of a large number of patients who harbor the broad tapeworm develop severe anemia. Some, but by no means all of these, develop what is to all appearances typical pernicious anemia. The majority, but not all, of those who present the blood picture of pernicious anemia show achlorhydria. From recent work it now appears that these cases also respond to the antianemic principle derived from liver.

It seems then that besides typical pernicious anemia undoubtedly due to the deficiency of the antianemic principle there is a group of cases in which a relative deficiency of this principle plus some other inciting factor such as digestive disturbance, incorrect diet, pregnancy or the broad tapeworm can produce a similar clinical picture. In the case of pernicious anemia, the administration of the antianemic principle apparently has to be continued throughout life. In the other instances, after the anemia has been cured and the inciting cause removed, the patients may remain well without further treatment.

Under the heading nutritional deficiencies are grouped a number of nutritional diseases often accompanied by anemia. In some of these, as the avitaminoses, specific vitamins are lacking; in others the exact causation is obscure. It is a question whether to place here certain infantile anemias, for example, the von Jaksch and the Cooley types; these undoubtedly have nutritional factors, but there may be infectious or constitutional factors also. These infantile anemias are in general severe and show an extremely pronounced bone marrow reaction with changes not only in the red cells but in the leukocytes. Probably because of the demands of growth the anemia very easily reaches an extreme degree.

It has been known to surgeons for a great many years that loss of all the bile through a postoperative fistula, if continued for a long time, produces a very severe grade of anemia. Exactly what constituent of the bile is important is not at all clear. The administration of bile or, according to a recent claim, of bile salts, seems to supply the deficiency.[24]

The blood picture in the rare cases of stenosis of the small intestine is said to resemble closely that of pernicious anemia,[25] but it is not probable that the pathogenesis is the same as that of pernicious anemia.[26]

19. Wood, E. L.: The Recognition of Tropical Sprue in the United States, J. A. M. A. **73:** 165 (July 19) 1919.
20. Evans, William, Lancet **1:** 14 (Jan. 5) 1929.
21. Peterson, Reuben; Field, Henry, Jr., and Morgan, H. S.: Liver Treatment in the Pernicious Anemia of Pregnancy, J. A. M. A. **94:** 839 (March 22) 1930.
22. Strauss, M. B.: Am. J. M. Sc. **180:** 818 (Dec.) 1930.
23. Wills, Lucy: Lancet **1:** 837 (April 16) 1932.
24. Balderston, S. V.: Anemia Associated with Biliary Fistula, Arch. Int. Med. **50:** 223 (Aug.) 1932.
25. Seyderhelm, R.; Lehmann, W., and Wichels, P.: Krankheitsforschung **4:** 263 (May) 1927. Little, W. D.; Zerfas, L. G., and Trusler, H. M.: Chronic Obstruction of the Small Bowel, J. A. M. A. **93:** 1290 (Oct. 26) 1929.
26. Meulengracht, E.: Acta. med. Scandinav. **72:** 231, 1929.

Nutritional anemia of adults is intended to include those cases of chronic hypochromic anemia in which a history of an extremely one-sided diet (usually consisting largely of starchy foods and lacking in proteins and frequently in vegetables) appears to play a large rôle in causation. These patients improve on iron but usually require correction of the dietary defect as well in order to insure complete recovery.

Aplastic anemias are divided into the so-called primary form and the cases secondary to known poisons. From the clinical similarities there is no doubt that the so-called primary cases are due to undiscovered agents which destroy bone marrow. It is important to know that the same toxic agent, as, for example, arsphenamine, or excessive radiation, may in some instances affect all the elements of the bone marrow, causing deficiency of the red cells, white cells and platelets (aplastic anemia). In other instances it may influence only one element; as for example, the leukocytes, producing pictures of acute leukopenia (agranulocytosis); or the platelets, producing acute hemorrhagic purpura.[27] This suggests—what has long been suspected clinically—that there is a close pathogenic relationship between the group of aplastic anemias, the agranulocytoses and the acute purpuras.

The group of anemias secondary to mechanical displacement of bone marrow needs little explanation. Osteosclerotic anemia is of two types: (1) the marble bone disease, a rare congenital disease beginning in childhood and going on to a grave anemia with fatal issue in spite of the myeloid changes in the spleen, liver and elsewhere in the body's effort to make up for the lack of bone marrow, and (2) osteosclerosis of adults, of unknown cause or occurring after prolonged inhalation of silica or other insoluble fine particles.[28]

The heading anemias due to interference with blood regeneration at some intermediate stage does not require much explanation. It is well known, of course, that material in the blood cells is to a certain extent broken up, conserved in the spleen and liver, and utilized in the reconstruction of blood. It is only natural, therefore, in many diseases affecting these organs that this function is seriously interfered with and that grave states of anemia result.[29]

The third great group of anemias, those due to hemolysis, are divided into (1) those in which the hemolytic process seems to be due to some inherited defect of the red blood cells themselves and (2) those due to extraneous toxic agents. There are two forms due to inherited defects; hemolytic icterus and sickle cell anemia; the clinical pictures are remarkably similar. The laboratory examinations of the blood reveal striking differences. In hemolytic icterus the fragility of the red blood cells, when tested with saline solutions, is greatly increased; in sickle cell anemia it is normal or the resistance is greater than normal. The correct diagnosis of hemolytic icterus is quite important because the sickness is often curable by splenectomy; unfortunately, this is not true of sickle cell anemia.

The second heading, toxic destruction of blood, includes a very heterogeneous collection of toxic agents. In some cases, as, for example, infection by hemolytic streptococcus or Staphylococcus aureus, definite hemolytic substances are known to be produced by the causative organisms. In others, such as malaria, destruction of red cells can be watched directly under the microscope. In many other instances, such as cancer, leukemia, nephritis and extensive burns, the intervention of a hemolytic substance is a justifiable assumption but has not been rigorously proved.

Acute febrile hemolytic anemia is an extraordinary and specific disease which has been recognized only in the past eight years.[30] It is a rapidly progressive febrile anemia with all the evidence of hemolysis (icterus, sometimes hemoglobinuria). Enlargements of the liver and spleen may occur. There is marked leukocytosis, and the blood is flooded with nucleated red blood cells. Untreated, it has a high mortality, but it responds remarkably well to blood transfusion.

THERAPY

It is interesting to note that almost all the diseases in which dietetic or medicinal therapy of anemia is effective fall in the first general group in the new classification; namely, the deficiences. It is impossible in the present article to discuss the treatment of anemia in all the diseases in which it occurs. I shall confine myself to discussing certain general principles regarding the use of iron, liver and blood transfusion.

1. *Iron.*—Vital as iron is, it is often not realized how little of it there is in the body. The whole body contains only about 3.5 Gm. of iron, less than the weight of a five cent piece. Of this, about 2.5 Gm. is in the form of blood hemoglobin. Iron is not peculiar to the hemoglobin-containing animals but occurs in all living things. The respiratory pigment present in practically all aerobic cells contains iron. There is only one atom of iron in each molecule of hemoglobin, according to the researches of Wilstatter, Anson and Mirsky and others, and it appears that one molecule of hemoglobin combines with one molecule of oxygen.[31]

There is some difference of opinion as to whether the effect of iron is due to stimulation of blood production or to the supplying of a real iron deficiency. The recent trend of opinion is strongly to the deficiency view. It is true that the doses which have to be given by mouth in order to obtain hemoglobin increase are enormously larger than the amount which is absorbed, and enormously larger than the minimal daily requirement of the body, which is only about from 6 to 12 mg. of iron. In all likelihood, however, this is due to the fact that iron is a substance which is absorbed with difficulty; only a small percentage of that taken by mouth is ever absorbed. Heath, Strauss and Castle [10] showed that with intramuscular injection of iron in hypochromic anemia patients the injected iron was almost quantitatively used in the making of hemoglobin. They found that the 32 mg. of iron which it was necessary to inject daily in the form of a 10 per cent solution of iron citrate, in order to get a maximal hemoglobin regeneration, was about equivalent in therapeutic effect to 1,000 mg. of iron taken by mouth in the form of 6 Gm. of iron and ammonium citrate. These authors, like Robscheit-Robbins, Witts and many others, found that while the oral dose required is large compared with the amount actually utilized by the body, there is always an optimal dose of iron by mouth; and increase of iron above this optimal dose does not lead to greater hemoglobin production.

How fast a hemoglobin production can one expect under the influence of iron treatment?

27. McCarthy, F. P., and Wilson, Robert, J.: The Blood Dyscrasias Following the Arsphenamines, J. A. M. A. **99:** 1557 (Nov. 5) 1932.
28. Chapman, E. M.: Am. J. M. Sc. **185:** 171 (Feb.) 1933.
29. Jones, C. M.: Blood Pigment Metabolism and Its Relation to Liver Function, Arch. Int. Med. **29:** 648 (May) 1922.
30. Lederer, Max: Am. J. M. Sc. **179:** 228 (Feb.) 1930.
31. Peters and van Slyke: Quantitative Clinical Chemistry **1:** 519, 1931.

This depends largely on the initial level of hemoglobin. When it is very low, the percentage increase is quite rapid if the therapy is having a proper effect, approximately 2 per cent of hemoglobin a day. As the percentage gets higher, the rate of increase slows down.

What is the best form of iron to use by mouth? All recent workers agree that organic iron compounds have no advantage over inorganic. Experience has shown that if the dose is very large it does not make much difference which form of inorganic iron is used. A number of careful studies, however, particularly those of Starkenstein,[32] indicate that ferrous iron is superior (in proportionate dose) to ferric. The solubility of the preparation undoubtedly plays a very decisive rôle, and this probably explains why the amount of iron needed in the form of reduced iron (which depends for going into solution largely on the hydrochloric acid of the stomach) is proportionately larger than other forms of iron. Thus Witts[33] showed that in hypochromic anemias the effective doses of metallic iron, ferric iron and ferrous iron are as given in table 3.

Closely connected with the question of the preparation of iron is the question of the hydrochloric acid of the stomach. Achlorhydria predisposes to iron deficiency. The poor absorption of iron in the absence of hydrochloric acid applies not only to inorganic iron as shown in the experiments of Mettier and Minot already referred to but also to the iron of vegetables as shown in the experiments of Mitchell and Miller.[34]

TABLE 3.—*Effective Doses of Metallic, Ferric and Ferrous Irons*

	Minimum Effective Dose	Iron Content
Reduced iron (metallic)	1.5–3.0 Gm.	1.2–2.4 Gm.
Iron and ammonium citrate (ferric)	4.0–8.0 Gm.	0.8–1.6 Gm.
Iron pill (ferrous)	2.0–3.0 Gm.	0.2–0.3 Gm.

Naegeli has shown cases in which blood regeneration on iron therapy commenced only when hydrochloric acid was added. On the other hand, as Witts points out, when the more soluble preparations of iron such as iron and ammonium citrate are used, hydrochloric acid is not needed and produces no increase of effect (excepting when minimal doses of iron are given). The so-called massive doses of iron which have been regarded as necessary, especially in the Scandinavian countries and in Germany, are reduced iron (i. e., metallic iron) and are massive not in the actual amount given (6 Gm., that is, 90 grains or more a day, according to Schulten[35]) but in the amount of iron, as the preparation is practically pure iron. For practical purposes the best preparations seem to be ferrous carbonate (in the form of the familiar Blaud's pill or saccharated ferrous carbonate powders) or, particularly for children because of its ease of administration, iron and ammonium citrate in 25 per cent solution. For infants, the dose of this citrate is from 5 to 10 grains (0.3 to 0.6 Gm.) a day; for adults, from 60 to 120 grains (4 to 8 Gm.).

Iron should be given by mouth and not by injection. Examination of the actual amount of iron in all the preparations that are suitable either for intramuscular or intravenous injection has shown that it is impossible to give sufficient amounts of iron unless the dose given is toxic or is extremely close to the toxic limit. Even if one were to give such a dose close to the toxic limit (and no one does), it would have to be injected daily. If given intramuscularly, it would produce local and, if given intravenously, severe general reactions. The only justification for the injection treatment of iron would appear to be in rare cases in which severe gastrointestinal disturbances make sufficient absorption from the intestine improbable. Iron seldom upsets the digestion, and even its reputed constipating effect is rather doubtful.

The recent experimental proof that minute amounts of copper are necessary in order to get the full effect of iron has led to the widespread addition of copper sulphate to iron in the treatment of hypochromic anemias. There is a good deal of doubt at present whether this is clinically necessary or justifiable. It must be remembered that the amount of copper needed is so small that its effect was discovered only when extraordinary and special precautions were made to remove all traces of copper from the food and from the administered iron. The ordinary preparations of iron and the ordinary diet probably contain all the copper that is needed; and as copper sulphate is somewhat upsetting to the digestion, it is questionable whether copper is a necessary addition to the therapeutic armamentarium.

The clinical reputation that some other metals, such as manganese and particularly arsenic, formerly enjoyed does not seem to be substantiated by recent research; while the last word has not been said, particularly about arsenic, at present its use in anemia is regarded as of questionable value.

2. The Antianemic Principle.—In the six or seven years since the introduction of the antianemic principle derived from liver for pernicious anemia and allied diseases there has been great improvement in the method of its use. The dosage is now standardized approximately by comparison with the effect to be anticipated from known amounts of whole liver taken by mouth. Thus the most widely used preparation, liver extract No. 343, is marketed in 5 Gm. vials each of which contains the equivalent of about 60 Gm. of liver (although it is prepared from 100 Gm. of liver, the difference being due to the loss in manufacture). With preparations made for intramuscular and intravenous use, it is customary for the manufacturer to state the approximate equivalent of liver from which the extract is derived. In the case of desiccated hog stomach and of other newer preparations derived from liver or stomach or both, the dosage has been arrived at by comparison with the therapeutic result of liver or the earlier liver extracts. Thus, one of the manufacturers has now a preparation to be given by mouth and derived from both liver and stomach which is claimed to be approximately three times as potent per unit of weight as the ordinary liver extract. The dose of liver or liver extract needed to reach and maintain a normal blood count varies from patient to patient. In a general way the equivalent of from 300 to 500 Gm. of liver a day is needed when the preparation is given by mouth.

Beebe and Lewis[36] at the Thorndike Laboratory in Boston divided 108 cases of pernicious anemia which they studied very carefully into four groups. The first and largest group of sixty-four patients required only from 100 to 400 Gm. equivalent a day to maintain a

32. Starkenstein, E.: Med. Klin. **25**: 1720 (Nov. 1) 1929.
33. Witts, L. J.: Proc. Roy. Soc. Med. **24**: 550 (March) 1931.
34. Mitchell, H. S., and Miller, L.: J. Biol. Chem. **85**: 355 (Dec.) 1929.
35. Schulten, Hans: München. med. Wchnschr. **77**: 355 (Feb. 28) 1930.
36. Beebe, R. T., and Lewis, G. E.: Am. J. M. Sc. **181**: 796 (June) 1931.

normal blood count after having once reached it. This group contained essentially the younger individuals (the average age being 45 years) and those showing few complications, such as infections, arteriosclerosis or neurologic manifestations. The second, the next largest group, thirty-one patients, were able to remain normal on an equivalent of from 500 to 1,000 Gm. This group averaged 60 years in age. A third group of five patients were not able to remain quite normal even on doses of liver up to an equivalent of 1,500 Gm. even when iron was added. The average age of this group was 69 years. The fourth group was composed of eight patients who were unable to reach normal on liver alone but did so when iron was added to their treatment. These cases all showed some dietary deficiency in their history and were probably combinations of pernicious anemia with a secondary nutritional anemia.

It is extremely important in each case to find out how much liver extract is needed to maintain a normal blood picture and then to give a dose decidedly above this amount, because it is known that the material is stored in the body, and it is also certain that intercurrent diseases such as infections and alimentary disturbances increase the need for the antianemic principle. The patient should be fortified against such occurrences. It has been noted by every one that the patients requiring very large doses are almost always those suffering from complications. This is particularly true of the neurologic complications; and, while it is impossible to produce regression of combined sclerosis when once established, by liver administration in any form, there is no doubt that sufficient liver to maintain a normal blood picture retards, if it does not arrest, the progress of such a sclerosis. On the other hand, carelessness of administration of liver in such cases frequently leads to rapid progress of the neurologic disease. It is possible that some of the cases of pernicious anemia that are refractory or that require excessive dosage are cases in which the antianemic substance is poorly absorbed from the gastro-intestinal tract. The recent introduction of liver extract which can be administered intravenously or intramuscularly may be a valuable asset in treating these cases.

Just as in the case of iron, so with the antianemic principle, the amount that has to be given by mouth is enormously greater than the amount that is actually absorbed and utilized by the body.

Gänsslen,[37] for example, found that 2 cc. daily of his purified preparation by intramuscular injection was the equivalent of from 300 to 500 Gm. of liver by mouth. This 2 cc. was prepared from only 5 Gm. of fresh liver, so that by this method a course of several months' treatment can be carried out with as much liver as the patient would otherwise consume in one day.

Castle and Taylor,[38] giving intravenously a purified form of fraction G (the equivalent of liver extract, No. 343) obtained the astonishing result that one injection containing the equivalent of 100 Gm. of liver was sufficient to produce one million red blood cells per cubic millimeter in ten days. The intramuscular and intravenous treatment of pernicious anemia, however, has many inconveniences and should be reserved for patients refractory to oral treatment or for persons who find it inconvenient on other grounds. It may be remembered also that Weinberg showed that liver extract is effective when given by rectum.

The antianemic substance of Minot in general is of use only in pernicious anemia and the related diseases. There is a good deal of clinical and experimental evidence that whole liver is of considerable use as an adjuvant to iron in many cases of other types of anemia. Whipple and Robscheit-Robbins have fractionated liver and have found that the fraction which contains the accessory substances is largely mineral and is quite different in its properties from the antianemic substance of Minot. Such an extract has recently been put on the market for the treatment of hypochromic anemia. There has not yet been sufficient clinical trial to make the results certain.

3. *Blood Transfusion.*—This is essentially an emergency measure. It is useful in patients acutely ill when first seen, in tiding very anemic patients over critical periods, such as the later months of pregnancy or surgical operations, and, in general, in all situations in which an extremely rapid improvement is urgent. This applies particularly to the first general group of anemias in my classification, the deficiency diseases, in which blood transfusion is needed practically only in such emergencies. In the second general group, particularly in the cases of bone marrow destruction, transfusion is almost the only means that are at present available of overcoming the anemia; and in instances in which there is any hope at all that the natural progress of the disease may reach an end (as, for example, in some cases of aplastic anemia, particularly those due to arsphenamine and allied substances), persistent use of blood transfusion will sometimes keep the patient alive until marrow regeneration occurs.

In the third group of anemias, those due to hemolysis, transfusion again is often of use as an emergency measure to tide the patient over until some other procedure can be used, such as splenectomy in the case of hemolytic icterus. In acute febrile hemolytic anemia, transfusion seems to be specifically curative. In almost all the other diseases included in the third group, medicinal or dietetic therapy, iron and liver extract fail completely, and the only real cure is the removal of the cause in those cases in which that can be accomplished.

1112 Park Avenue.

37. Gänsslen, M.: Klin. Wchnschr. **9**: 2099 (Nov. 8) 1930.
38. Castle, W. B., and Taylor, F. H. L.: Intravenous Use of Extract of Liver, J. A. M. A. **96**: 1198 (April 11) 1931.

Practice From the Homes.—It is stated that the services of the family physician can be improved by coordinating him in a group together with the specialist, in association with and under the control of a non-profit-making corporation, such as a hospital. The assumption is that the consumer requires in a majority of instances the services of various specialists and of expensive plant, this making it more economical to bring at once the family physician and his clients to a central point where these are available. Moreover, it is also assumed that by such organization the requisite service could be provided far more economically than is done now. The majority of family physicians at the present time practice from their homes, where the overhead for office rent, transportation and incidental expenses is to a considerable extent included in the necessary charges for shelter, transportation and other needs of himself and family. Moreover, the expense of setting up the necessary office equipment and apparatus for the care of the illness with which he deals is minimal. In other words, the charges of plant are a very small fraction of the cost of his service. To bring him into a group renders these fixed charges a major fraction of the cost of his services, and the net result must be either increased charge for service or less net return to the physician.—Harvey, S. C.: Oikonomia Medika, *Yale J. Biol. & Med.* **5**:323 (March) 1933.

THE ECONOMIC BURDEN OF OSTEOMYELITIS

CALEB S. STONE, JR., M.D.
UNIVERSITY, VA.

The suffering, the prolonged hospitalization and the great cost of osteomyelitis are obvious to those who have followed these patients through their hospital courses. There have been no studies that have brought out the marked economic loss entailed by this disease. A survey of the cases of osteomyelitis treated at the University of Virginia Hospital presents such a striking demonstration of this enormous economic burden that a presentation of the figures is thought to be worth while. It is particularly worth while if it can be felt that earlier diagnosis and treatment can help decrease the expense to the patient and to the hospital. The moral of this report will then become obvious.

TABLE 1.—*Classification of Cases*

Group A	Patients hospitalized first at University of Virginia Hospital; treated at home first but without operation on the bone	154 cases
Group B	Patients hospitalized elsewhere for treatment first, including 30 patients operated on at home	98 cases

This study is limited to those cases of acute, pyogenic osteomyelitis of hematogenous origin, usually seen in children and most frequently caused by the staphylococcus. Other bone infections, including tuberculosis, traumatic osteitis, and osteitis originating in arthritis, are not included.

The economic cost of any disease is made up of a number of different factors, which may be divided into those affecting the hospital and those affecting the patient and, through the patient, the state; the latter is by far the most important. In the case of the well-to-do patient, the hospital cost of any illness is generally absorbed by the patient or his family. With increasing degrees of poverty, the burden rests more and more on the hospital. It is the general impression, and the figures given later bear this out, that osteomyelitis is rare in the well-to-do, and that it is usually seen in more or less destitute individuals. In the consideration of osteomyelitis, therefore, the cost to the hospital becomes a major factor.

The hospital cost, exclusive of the physician's charges, includes:

(*a*) The cost of each hospital day.
(*b*) The cost of drugs and dressings.
(*c*) The cost of special procedures; i. e., the operating and plaster room charges.
(*d*) The cost of laboratory procedures, including roentgenograms.

The expense to the patient is made up of:

(*a*) The cost of medical attention, including the hospital bill.
(*b*) The loss of time from work due to the acute illness.
(*c*) The total loss of time from work, and the loss of quality of work because of prolonged chronic illness and deformity.
(*d*) In the case of children, the economic loss due to interference with education.
(*e*) In addition, a loss to the community through death. This will be seen to be of importance.

From the Department of Surgery and Gynecology and the University Hospital, University of Virginia School of Medicine.

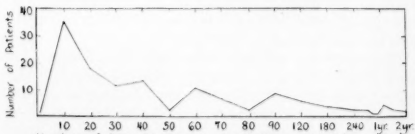
The figures to be presented will bear especially on the hospital cost and on the cost to the patient of the acute illness. They will also suggest something of the economic loss from chronic disease and the resulting deformities.

Up to January 1930 there were 252 cases of osteomyelitis treated in the University of Virginia Hospital. These have been divided into two groups, as shown in table 1.

Because of lack of accurate knowledge of previous treatment, the cases in group B cannot be analyzed closely with profit. They have been tabulated in order to bring out certain points to be discussed later. The chief facts for the present thesis are to be gathered from group A, which has been analyzed in detail in table 2.

In table 2 the column headings are self-explanatory with the exception of those in columns 8 and 9; by total cost to the patient is meant the total of bills rendered the patient on discharge. To determine the hospital cost to the patient, ten unselected records were examined. Some of these patients were paying the full ward rate and some were paying a smaller rate. The total number of hospital days for this group was divided into the total amount charged this group. The factor thus obtained, $2.19, is considered a fair average of the daily hospital charge for patients in this group, including the charges for dressings and roentgenograms. To determine the total hospital bill for each patient, the number of hospital days has been multiplied by this factor. In this entire group there was only one patient (private) who was charged for the medical attention received.

The total figures show that for an average stay in the hospital of 94.6 days, the average cost to the patient was $207.17. Over a long period of time, it has been found that the average per capita cost at the University Hospital is about $4 a day. This is the basic figure used in estimating the cost to the hospital, shown in column 9 (table 2). It is obvious that it costs the hospital $378.49 to care for a patient for 94.6 days, though this patient has been charged only $207.17. Assuming that the patient with osteomyelitis pays his entire bill, there is a loss to the hospital that averages in this series $161.32. Unfortunately, such an assumption is entirely unwarranted in this institution. It has been stated that most children with this disease come from families unable to bear this burden, and when this is the case there is an additional loss to the hospital. It is difficult to estimate this amount. The figures shown in table 3 will give some idea of this additional cost. Nineteen unselected cases from this group were investigated. Of these, in seven cases the hospital frankly assumed the entire burden. Of the remaining twelve patients, three have not paid bills. Comparing the amount paid to the cost to the hospital of these


Number of Patients
40
30
20
10
10 20 30 40 50 60 70 80 90 120 180 240 1yr 2yr
Number of Days Ill Prior to Admission to the Hospital

Duration of illness prior to admission to the hospital.

patients as estimated in table 2, it is found that 82.9 per cent of the cost of hospitalization is borne by the hospital alone. These facts are shown in table 3.

The administration of the hospital sees no prospect of diminishing this loss in these instances. If this percentage carries through the entire series, it becomes clear that the net cost to the hospital shown in column 10 is grossly underestimated. It should by this reasoning approximate $350 per patient.

In estimating the money loss to the patient from the acute illness, one must consider other factors besides cal attention has been necessary during this interval. The average number of previous hospital admissions had been one plus. Thirty of these patients had had some type of operation directed at the bone, even though they were not hospitalized, and are therefore included in this group. The previous experience of these patients compares very closely with that of the patients in group A. This table shows that the chance of additional hospitalization averaging 53.6 days, at an average cost of $147.54, faces the members of group A.

TABLE 2.—*Analysis of Group A*

Bone Primarily Involved	Number of Cases	Number of Cases with Involvement of Joint	Days of Illness at Home Before Admission to Hospital: Total for Group	Days of Illness at Home Before Admission to Hospital: Aver. per Patient	Number of Admissions: Total	Number of Admissions: Average	Number of Operations: Total	Number of Operations: Average	Number of Casts	Number of Days in Hospital: Total for Group	Number of Days in Hospital: Aver. per Patient	Total Cost to Patients of Hospitalization: Total	Total Cost to Patients of Hospitalization: Average	Cost to Hospital: Total	Cost to Hospital: Average	Loss to Hospital, Assuming All Bills Paid: Total	Loss to Hospital, Assuming All Bills Paid: Average	Deaths: Number	Deaths: Per Cent	Healed After Amputation: Number	Healed After Amputation: Per Cent	Healed with Shortening: Number	Healed with Shortening: Per Cent	Healed with Ankylosis: Number	Healed with Ankylosis: Per Cent	Total Deformities	Percentage of Deformities
Tibia	67	10	5,370	80.1	103	1.5	107	1.6	13	5,492	81.9	12,027.48	179.36	21,968	327.88	7,103.0	148.52	4	5.9	2	2.9	2	2.9	6	8.9	10	14.92
			Longest, 2 yrs. Shortest, 4 da.																								
Femur	46	5	3,156	68.6	69	1.5	79	1.7	11	5,558	120.8	12,172.02	264.55	22,232	483.30	7,402.0	218.75	9	19.5	3	6.5	2	...	5	10.8	10	21.74
			Longest, 2 yrs. Shortest, 1 da.																								
Humerus	19	5	1,065	56.0	36	1.5	39	2.5	2	2,325	122.3	5,091.75	267.83	9,300	489.47	3,087.5	221.64	1	5.3	0	0.0	1	5.3	5	26.3	6	31.57
			Longest, 1 yr. Shortest, 4 da.																								
Other long bones	6*	1	90	15.0	10	1.6	14	2.3	0	366	61.0	791.54	133.59	1,464	244.00	409.0	110.41	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
			Longest, 42 da. Shortest, 3 da.																								
Miscellaneous	16†	5	1,512	94.5	20	1.3	22	1.4	0	831	51.9	1,819.89	113.66	3,324	207.75	1,237.0	94.90	1	6.25	2	12.5	0	0.5	0	0.0	2	12.5
			Longest, 330 da. Shortest, 4 da.																								
Totals	154	26	11,193	72.6	238	1.5	261	1.6	26	14,572	94.6	31,912.68	207.17	58,288	378.49	19,328.5	161.32	15	9.7	7	4.5	5	3.2	16	10.4	28	18.11
			Longest, 2 yrs. Shortest, 1 da.																								

* Ulna, 1; radius, 2; fibula, 3.
† Astragalus, 1; os calcis, 4; metatarsal, 5; pubis, 1; scapula, 1; rib, 4.

the hospital cost. Column 3 of table 2 shows that the patients of this group were ill at home for an average of 72.6 days. This figure is high on account of a few patients who were ill over a year. The chart shows that nearly half of these patients were admitted within three weeks of the onset of their illness. Though no accurate estimate of the cost of medical and nursing care during this period of home treatment can be determined, it is an item of no small amount, which must be included in the total cost to the patient. Even though the patient or his family cannot pay the hospital bill, the average amount of $207.17 must be charged to him. Parenthetically, it may be remarked that, from the clinical point of view, it is appalling to find about three fourths of these patients sent to the hospital after a week of illness. This fact, of course, has its economic sequel, as will be pointed out.

The direct money loss to the patient or his family, which has been defined as closely as possible in the preceding paragraphs, is not the entire direct money loss. Discharge from the hospital rarely means cure. To gather some idea of what this later loss may be, one must turn to the cases admitted to this hospital after treatment elsewhere, often years previously; namely, those of group B in table 1.

Table 4 presents a partial analysis of this group; it is to be noted that the disease has lasted an average of twelve years and seven months. Doubtless, some medi-

The economic burden arising from loss of working time must next be discussed. Most of the patients in group A are children. It is difficult to attach any monetary value to their time. However, the services of a child in the home, on the farm or in industry are valuable, and particularly is this true in families in which poverty is present. With an average duration

TABLE 3.—*Cost to Hospital of Nineteen Unselected Patients*

Number of Patients	Number of Patients Charged Full Ward Rate		Number of Patients Charged Smaller Rate		Number of Patients Admitted as Free Patients	Total Money Paid by Group	Cost of Group to the Hospital	Loss to the Hospital
19	9		3		7	$1,162.75	$6,788.00	$5,625.75 82.9%
	Bill paid, 6	Bill never paid, 3	Bill paid, 3	Bill never paid, 0				

in the chronic cases of over twelve years, many of these children are still handicapped when the self supporting period of life is reached.

The chronicity of osteomyelitis is well known. The loss of time because of reopening sinuses, or the protracted drainage of wounds cannot well be measured, though that loss must be great in a condition that has persisted, as in group B, over an average period of more than twelve years.

Nor can the economic waste due to crippling deformity be measured. In a group of people most of whom find their livelihood in manual labor, amputation, ankylosis of a joint or the shortening of an extremity may mean the difference between self support and dependence. Table 5 shows the incidence of these deformities in group A as compared to group B. It is perhaps striking that while ankylosis occurs in 10.4 per cent of the cases during the early acute infection, it occurs in 12.2 per cent of the late cases in group B. That deformities, escaped at first, may come later, during acute recurrences of the disease, only serves further to increase the ultimate burden of osteomyelitis. Nearly 20 per cent of this series of acute cases have a majority of cases, then, there has already been considerable bone destruction before treatment is begun, and, regardless of the type of treatment, the disease usually runs a protracted course.

It has been repeatedly stated that early diagnosis and immediate operation offer the best chance of minimizing the protracted period of disability, as well as decreasing the number of deformities of the late chronic form of the disease. To emphasize the importance of early intervention, many experienced surgeons have stated that, for each hour's delay in operating, the course of the disease is prolonged by from four to six weeks. In spite of this general attitude among surgeons toward osteomyelitis, few patients are hospitalized early. In this entire series, only one patient was admitted on the first day of the disease. In the

TABLE 4.—*Analysis of Group B*

Total Cases	Time Since Onset of Initial Acute Infection: Total	Time Since Onset of Initial Acute Infection: Average per Patient	Previous Hospital Admissions: Total	Previous Hospital Admissions: Average per Patient	Previous Operations: Total	Previous Operations: Average per Patient	Number of Days in This Hospital: Average Number per Patient	Admissions to This Hospital, Average per Patient	Number of Operations, Average per Patient	Expense in This Hospital, Average per Patient	Mortality, per Cent	Ankylosis, per Cent	Amputations, per Cent	Shortening, per Cent	Total Deformity, per Cent
98	1,232 Yrs. 6 Mos.	12 Yrs. 7 Mos.	100	1+	102	1+	53.6	1.3	1.3	147.54	3.06	12.2	5.1	2.04	19.38

Longest time = 66 Yrs.
Shortest time = 1 Yr.

crippling deformity. With the 10 per cent of deaths, this places nearly a third of the victims of this disease outside the class of normal individuals.

One other element in the economic burden to the individual must be considered. The usefulness of the man depends largely on the completeness of his education during childhood. The average total loss of time during the early period of the disease, as shown in table 2 (group A), is 5.5 months, which is the equivalent practically of an entire year in school. The protracted nature of the disease, the frequency of recurrence necessitating hospitalization, as indicated in table 5, may well deprive a child of most, if not all, of his early schooling. Again this loss cannot be measured.

Lastly, the money cost to the family through the death of a child: Dublin and Lotka [1] have estimated the cost of bringing a child up to adolescence in a family whose income is about $2,500 a year. The total cost of bringing the child up to 18 years is given as $10,485. In group A of this series, the average age of these patients at the onset of their disease is 11 years 8.9 months, roughly 12 years. In table 2 on page 39 of Dublin and Lotka's book is given the total cost of bringing a child up to this age, which is $5,896. In preparing these figures, the authors have made an allowance for the cost of illness. This figure may be taken, then, to represent the total cost of the child dying at the age of 12 years.

COMMENT

The measurable factors in the economic burden imposed by osteomyelitis, namely, the costs of hospitalization, which have been presented, and the other factors not so closely measurable, which have been enumerated and their degrees suggested by related figures, present a total picture that is appalling. When to it is added the patient's pain and the parental worry and grief, osteomyelitis presents itself as a major scourge. It is obviously the duty of every practitioner of medicine to bend every effort in preventing its ravages.

It is impossible to show by this study that early diagnosis with prompt and adequate surgery would decrease the morbidity of osteomyelitis. Those variable factors, the virulence of the infecting organism and the resistance of the host, will always influence the course and outcome of any individual infection. However, all surgeons have seen a few early cases that have made a prompt and complete recovery following early intervention. There being no other means now at hand whereby the length of the disease may be shortened or the economic burden lightened, I feel justified in renewing the plea for early diagnosis.

TABLE 5.—*Percentage of Cases Terminating in Death or with Deformity*

	Group A	Group B
Death	9.7	3.06
Ankylosis	10.4	12.20
Amputation	4.5	5.10
Shortening of extremity	5.2	2.04
Total deformities	18.1	19.38

SUMMARY

1. The course of pyogenic osteomyelitis is prolonged.

2. Figures have been presented to show the cost to the hospital in caring for patients with this disease as well as the cost of medical attention and hospital care to the patient.

3. There is an additional economic burden to the patient because of loss of time due to the initial acute infection, loss of time and loss of quality of work due to prolonged chronic illness, and frequently deformity.

4. In the case of children, there is a loss due to interference with education.

5. Few cases are seen early. Earlier diagnosis is suggested as the only means at hand for decreasing the burden of osteomyelitis.

1. Dublin, L. I., and Lotka, A. J.: The Money Value of a Man, New York, Ronald Press Company, 1930, p. 22.

THE 1932 THALLOTOXICOSIS OUTBREAK IN CALIFORNIA

JAMES C. MUNCH, PH.D.
GLEN OLDEN, PA.
HYMAN M. GINSBURG, M.D.
AND
C. E. NIXON, M.D., PH.D.
FRESNO, CALIF.

Following the exposure of human beings to various products containing thallium, prepared for rodenticidal or clinical use, a number of untoward effects have been reported during the last few years. In addition to alopecia, the principal effects reported have been stomatitis and gastro-enteritis, diarrhea and constipation, peripheral neuritis, retrobulbar neuritis and endocrinologic disturbances.[1] In 1924, an intensive study of the pharmacology of thallium was instituted by the Bureau of Biological Survey on animals which led to the development of an antidote for thallium poisoning and to definite information regarding its physiologic actions.

"Thalgrain" was prepared by official agencies to contain 1 per cent of thallium sulphate and distributed in certain areas in ten counties in California for assistance in controlling ground squirrel infestation.[2] Following its use on a small scale in 1925, the amount of such material has been increased annually until 1928, since which time progressively smaller quantities have been used.

The antidotal treatment developed had been used on animals but had never been tested on human beings until the present outbreak. Other investigators have studied the treatment of thallotoxicosis. Sodium thiosulphate has been reported as successful, or at least as useful,[3] although other workers have denied obtaining any benefit.[4] Pilocarpine has been used alone [5] or in combination with sodium thiosulphate.[6]

In our studies on antidotal treatment, the reasoning followed our knowledge of the chemical behavior of thallium compounds: 1. Thallous sulphate is readily soluble in water (4,000 mg. per liter), whereas thallous iodide is very much less soluble (125 mg. per liter).[7] Experiments were undertaken with intravenous injections of sodium and potassium iodide with the hope of converting the soluble thallous compounds into the insoluble iodide. To avoid the depressant action of potassium salts, sodium iodide was preferred, even though less available. To follow the degree of fixation, the decrease or disappearance of thallium from the urine was determined by the changes in intensity of green color when the residue from the twenty-four hour urine was brought in contact with a nonluminous flame. 2. After fixation, elimination of the thallous complex was produced by intravenous or oral administration of sodium thiosulphate. When too large a dose was given, symptoms of acute thallium poisoning developed, which were removed by another injection of sodium iodide. 3. Disturbances of calcium metabolism, possibly related to parathyroid injury, have been reported. The injection of soluble calcium salts was therefore instituted. 4. To combat endocrinologic depression, which had been frequently observed, pilocarpine was used.

HISTORY OF OUTBREAK

With the exception of an outbreak of thallium poisoning in California in March, 1931, which was not diagnosed as such at the time but in which the cases were treated for "heavy metal poisoning," with complete recovery of five adults and the death of a 15 months old infant who failed to show characteristic thallium effects on postmortem examination,[8] no outbreak of thallium poisoning has occurred in this country.

Fig. 1.—Container and labels placed on thalgrain.

In this outbreak, a Mexican laborer illegally procured a 100-pound bag of thalgrain (fig. 1) from a locked official warehouse. The grain was distributed to several Mexican families, ground, and the barley flour used in the preparation of tortillas. The various housewives noticed that the material had a peculiar coating and contained discolored grains and débris. Tortillas made from the material fell apart. To correct this, some sound wheat flour was mixed with the thalgrain barley flour and the material eaten by two families.

1. A family in Selma, consisting of at least fourteen persons, consumed from one to four tortillas each at the evening meal, January 12. Two children, who had eaten the most, were ill the next morning, so the uneaten tortillas and the remaining grain were buried. Thirteen members were hospitalized in the General

From the Bureau of Biological Survey, Washington, D. C., and the General Hospital of Fresno County.

1. Munch, J. C.: The Toxicity of Thallium Sulphate, J. Am. Pharm. A. **17**: 1086-1093, 1928. Buschke, A., and Peiser, B.: Die biologischen Wirkungen und die praktische Bedeutung des Thalliums, Ergebn. d. allg. Path. u. path. Anat. **25**: 1-57, 1931. Kaps, L.: Kriminelle Tödliche subakute Thallium-Vergiftung, Wien. klin. Wchnschr. **40**: 967-970 (July 28) 1927.

2. Kellogg, E. S.: The California Ground Squirrel Control Program, Spec. Pub. 109, Dept. of Agri., State of California, 1931.

3. Bogdanov, S., and Lasko, N.: Zur Thalliumbehandlung der Pilzerkrankung und zur Behandlung von Thalliumszwischenfällen mit Natrium-Thiosulfat, Vrac. Delo **11**: 304-306, 1928. Mrongowius, J., and Duchan, G.: Zur Frage der Vermeidung der Komplikationen bei der Thallium-Therapie, Dermat. Wchnschr. **87**: 1834-1835 (Dec.) 1928. Caluzzi, N.: Il tiosolfato di sodio quale antidoto del tallio nelle cure epilatorie, Dermosifilografo **4**: 399-402 (Aug.) 1929.

4. Buschke, A.; Duchan, G., and Joseph, A.: Ueber die Anwendung des Natriumthiosulphate zur Verhütung der Komplikationen bei der Thalliumtherapie, Dermat. Wchnschr. **87**: 1835-1837 (Dec. 1) 1928.

5. Lenartowicz: Thalliumacetat als Epilationsmittel, Przegl. dermat. **22**: 256-270, 1927 (cited by Buschke and Peiser.[4]).

6. Mrongowius and Duchan.[3] Caluzzi.[3]

7. Mellor, J. W.: A Comprehensive Treatise on Inorganic and Theoretical Chemistry, London, Longmans, Green & Co. **5**: 406-479, 1924.

8. Robinson, Joseph, and Tock, E. W.: Personal communications to the authors.

Hospital of Fresno County between January 14 and January 24. The details of the symptoms, treatment and outcome are given in table 1. Two mothers and four children died before January 28. The patients refused to cooperate, and incomplete histories were obtained. It was not until January 22 that friends of the patients brought in some of the tortillas and with the assistance of County Agricultural Commissioner Roullard, Chief State Rodent Control Officer Jacobsen, and the chemical laboratories of the California State Department of Agriculture, and the bureau, the material was identified as thalgrain. A preliminary report on these patients has been published.[9]

2. A family in Tipton, consisting of at least seventeen persons, consumed an unknown number of tortillas daily for a week. A girl, who ate about three times as many tortillas as any of the others, was hospitalized, lost the cranial hair and developed a unilateral left-sided paralysis. The same treatment was used by the superintendent of the Tulare Hospital, Dr. Kohn, as was used in the Fresno hospital (table 1). In all, over thirty-one persons were exposed, fourteen were hospitalized, and six died from acute thallium poisoning. Another death occurred almost two months later, but it was not certain that thallium was responsible. Symptoms of thallium poisoning developed in twenty-two persons; alopecia (fig. 2) and pains in the legs and feet were the chief symptoms.

Fig. 2.—Complete loss of cranial hair following consumption of tortillas prepared from thalgrain.

TREATMENT

The general principles of the treatment of thallium poisoning in man are:

1. If the patient is seen early, the stomach should be emptied by lavage or by use of emetics (mustard or apomorphine). Cathartics are used to eliminate unabsorbed material from the gastro-intestinal tract. It may be dangerous to use cathartics that contain sulphates, since the insoluble thallium compounds fixed in the gastro-intestinal tract may react with sulphates and become soluble.

2. In the acute cases, when the patient is in shock, 25 Gm. (50 cc.) of dextrose should be given intravenously, heat applied to the extremities, and caffeine sodiobenzoate, epinephrine, or aromatic spirit of ammonia given, as deemed necessary.

3. Fixation should be started immediately after it is learned that thallium poisoning is being treated. Intravenous injections of iodides are indicated to convert the toxic soluble thallium salt to a practically insoluble iodide. Owing to its depressant action, potassium iodide should not be used if sodium iodide is available. From 5 to 15 grains (0.3 to 1 Gm.) of sodium iodide should be given intravenously daily and, at the discretion of the attending physician, the dose may be increased to from 25 to 40 grains (1.6 to 2.6 Gm.), or even more. The iodides are continued until urinary examinations reveal that practically no thallium is being excreted (the residue obtained by flaming the residue of a twenty-four hour sample gives only a slight green color).

4. For elimination, intravenous injections of sodium thiosulphate may be given. This should not be given by mouth. The object is to convert a nonsoluble thallous iodide gradually to a soluble thallous compound, and to remove it rapidly from the body. A dose of from 0.3 to 1 Gm. may be given to an adult, and proportionate doses to children. Twenty-four hour urine samples are collected daily and the flame test applied to make certain that too rapid elimination is not produced. Should thallotoxicosis again develop (as a result of too rapid mobilization of bound thallous iodide) with as small a dose of sodium thiosulphate as 0.3 Gm., from 0.3 to 1 Gm. of sodium iodide should be injected intravenously and natural elimination awaited.

If thallotoxicosis does not develop and the urine test shows very little thallium following the initial thiosulphate treatment, then it is recommended to increase cautiously the thiosulphate, very careful checks being made on the urine. Injections of thiosulphate are discontinued when the daily flame test for a twenty-four hour urine, over a period of three days, shows that elimination is practically complete.

5. To promote secretory activities, pilocarpine hydrochloride in doses of 5 mg. is given to hospital patients, beginning about the third or fourth day, and continued at the discretion of the attending physician. It should not be given to ambulatory patients or to patients suffering from pulmonary congestion.

6. Disturbances in calcium metabolism are treated by the use of from 20 to 40 grains (1.3 to 2.6 Gm.) of calcium salts (chloride, lactate or gluconate) given daily during the period of elimination and continued at the discretion of the attending physician.

7. Purely symptomatic treatments indicated are:

(*a*) One drachm (4 cc.) of dilute hydrochloric acid before each meal to overcome the achlorhydria or hypochlorhydria found in thallium poisoning.

(*b*) Fluids freely, especially milk, which is rich in calcium salts.

(*c*) Bland ointments for the dermatitis about the mouth.

(*d*) Amytal, 0.1 Gm.; sodium bromide, 1 Gm.; codeine or morphine for restlessness and pain.

(*e*) Cod liver oil and nutritious food.

(*f*) Mechanical restraints, if necessary, in mental cases.

(*g*) Sponges for high temperature.

9. Ginsburg, H. M., and Nixon, C. E.: Thallium Poisoning, J. A. M. A. **98**: 1076-1077 (March 26) 1932.

TABLE 1.—*Symptoms, Treatment and Outcome of Thallotoxicosis Outbreak in Selma Family*

Case	Patient	Sex*	Age, Years	Ingested Thallium (1932)	Onset of Symptoms (1932)	Admission to Hospital (1932)	Symptoms and Observations	Treatment	Course
1	N. N.	♀	32	1/12	1/13	1/14	Nausea; vomiting; epigastric pains; pains and paresthesia in extremities; reflexes hyperactive; blood pressure 120/84, alopecia; stomatitis; strabismus; ptosis; difficulty in speech; myoclonic twitching; delirium; coma	Before diagnosis of thallium poisoning; eggs; milk; fluids; castor oil; potassium citrate; morphine; dextrose intravenously; sodium thiosulphate After diagnosis of thallium poisoning; intravenous dextrose; saline colonic flushes; intravenous calcium chloride; parathyroid extract; potassium iodide (1 dose); fluids freely	Died 1-26
2	Y. N.	♂	34	1/12	1/13	1/14	Nausea; vomiting; pain in epigastrium and extremities; reflexes hyperactive; salivation; stomatitis; ptosis; alopecia; patient was talkative and irrational; optic atrophy; delirium; coma; blood pressure 160/70; blood and urine negative	Before diagnosis: as in case 1 After diagnosis: 62 grains of sodium iodide intravenously, daily; calcium lactate; fluids and dextrose; after 5 days, sodium thiosulphate; calcium gluconate, dilute hydrochloric acid; fruit juices; milk and fluids; pilocarpine, 1/12 grain; (1 dose) (sudden exacerbation of thallotoxicosis caused stopping of thiosulphates and administration of iodides for three days); cod liver oil and nutritious foods	Thallium symptoms disappeared by 2-7; died 2-25, from leptomeningitis
3	I. N.	♂	10	1/12	1/13	1/14	Pain in extremities and abdomen; nausea; vomiting; alopecia; stomatitis; ptosis; difficulty in deglutition; convulsions; irritable encephalitic-like picture; spinal puncture negative; bluish line at gums; myoclonic twitchings; stupor; coma	Before diagnosis: as in case 1 After diagnosis: as in case 7	Died 1-24
4	A. D.	♂	33	1/12	1/13	1/14	Pain in the extremities and abdomen; tingling in extremities; vomiting; hyperesthesias in fingers and toes; foul breath; salivation; alopecia; myoclonic twitchings; dilatation of pupils; conjunctivitis; urine, blood and Wassermann negative; patient irrational; psychosis; involuntary bowel movements; spinal fluid negative; blood pressure 150/110	Before diagnosis as in case 1 After diagnosis: potassium iodide in doses of 5 minims for first day and sodium thiosulphate; on 2d day to 7th, calcium gluconate; dilute hydrochloric acid; sodium bromide; fluids and milk	Discharged 3-8; physical condition good; mental symptoms present
5	C. D.	♀	29	1/12	1/13	1/14	Pain and numbness in extremities; abdominal cramps; dilated pupils; alopecia; coma	Before diagnosis: as in case 1 Transferred to another hospital, Jan. 5; no symptomatic or general treatment given	Died 1-28
6	B. R.	♂	43	1/12	1/13	1/19	Pain in extremities and abdomen; nausea; vomiting; hyperesthesias; stomatitis; alopecia; restlessness; gums purplish; 2.0% eosinophils; blood pressure 145/92	Before diagnosis: as in case 1 After diagnosis: potassium iodide for 1 day and then sodium iodide for 5 days; calcium lactate; intravenous dextrose; milk; fluids; after 5 days sodium thiosulphate; calcium gluconate; dilute hydrochloric acid; fruit juices; cod liver oil	Discharged 2-13
7	L. N.	♀	7	1/12	1/13	1/20	Pain and numbness in extremities; nausea; epigastric pain; alopecia; disturbance of consciousness; choreiform twitchings; convulsions; pulmonary symptoms; blood and urine negative; spinal fluid under slight pressure; fluid clear	Colonic saline flushes; subcutaneous saline solution with 5% dextrose; potassium citrate; codeine for pain; intravenous calcium chloride; potassium iodide, 1 minim; magnesia magma; ether for convulsions	Died 1-23
8	M. N.	♂	6	1/12	1/13	1/21	Pain, tenderness and numbness in extremities; abdominal cramps; stomatitis; salivation; ptosis; vomiting; strabismus; myoclonic twitchings; alopecia; convulsions; coma; blood and urine negative	As for case 7 except that no ether was used	Died 1-23
9	L. N.	♀	5	1/12	1/13	1/21	Pain in extremities and abdomen; vomiting; stomatitis; alopecia; convulsions; pulmonary symptoms; ptosis; pupils dilated; strabismus; involuntary bowel movements	As for case 7 except that no ether was used	Died 1-24
10	I. D.	♂	7	1/12	1/13	1/24	Alopecia; thallium in urine; blood and urine negative; (no thallium in urine on discharge)	Intravenous dextrose; calcium lactate; magnesium chloride; sodium thiosulphate, one dose of potassium iodide; 0.5 cc. parathyroid extract; intravenous sodium iodide 3 days, then sodium thiosulphate; calcium gluconate; dilute hydrochloric acid, ovoferrin; coco emulsion	Discharged 2-12
11	V. D.	♂	9	1/12	1/13	1/24	Pain in extremities and abdomen; alopecia; lethargy; ptosis; strabismus; paresis of extremities; blood and urine negative; photophobia; tuberculin test negative; thallium in urine; urine negative for thallium on discharge	As for case 10, with addition of codeine; pilocarpine, grain 1/12	Discharged 2-12
12	F. G.	♀	19	1/12 to 1/22	1/20	1/24	In Tulare hospital, symptoms and observations as in preceding eleven cases, with an addition of unilateral paralysis on left side; urine contained thallium on 7th day; none on 14th day	Sodium thiosulphate for 10 days	Discharged 2/10

* In this column, ♂ denotes male; ♀, female.

PATHOLOGIC OBSERVATIONS

Necropsies were conducted on the patients who died.

Blood.—Gradual erythropenia and leukocytosis with the appearance of normoblasts, a decrease in polymorphonuclear leukocytes and eosinophilia have been reported.[10] Basophilic stippling has been reported[11] and denied.[12] In our cases there were no striking changes in the blood picture. The proportion of eosinophils and basophils varied from zero to 2 per cent. There was no increase in the monocytes. Basophilic stippling was not found.

Gastro-Intestinal Tract.—Confirming reports in the literature,[13] moderately severe gastro-enteritis developed. Postmortem examinations revealed hyperemia and punctate hemorrhages in the mucosa of the stomach and upper intestinal tract, accompanied by swelling and variations in staining of the mucosal cells, most marked in the superficial layers.

Kidneys and Urine.—Glomerulonephritis,[14] degenerative lesions of the kidney,[15] and necrosis [16] have been reported. In our cases there was a slight or moderate increase in albumin and in hyaline and granular casts. Red blood cells were present in only one instance. Thallium was found in the urine as long as three weeks after the tortillas had been consumed. At necropsy, cut sections of the kidneys were dull red and showed impairment of the anatomic markings. Microscopic sections presented marked hyperemia, cloudy swelling and degenerative changes of the cells of the glomeruli and the tubules.

Lungs.—Bronchitis, edema and bronchopneumonia have been reported.[17] In our cases no striking clinical changes were observed before death. At necropsy, cut sections were dark red, and large amounts of frothy, rather viscid, faintly blood-tinged fluid escaped from the cut bronchi following compression. Microscopic examinations showed the alveoli distended with serum, marked hyperemia, and pigments both free and in large mononuclear cells. A few areas presented the microscopic picture of bronchopneumonia.

Liver.—Swelling of the reticulo-endothelial cells [18] and fatty degeneration [19] have been reported. In these cases there were no clinical indications of liver involvement before death. On necropsy, extensive injury was observed: The livers cut with increased resistance, and the cut sections were grayish yellow or yellow. Microscopically there was a marked fatty infiltration of the liver cells with a tendency to central necrosis.

Endocrine Glands.—Hyperemia, congestion and atrophy of the thyroid,[20] marked vacuolization of the suprarenal cortex,[21] and a decreased epinephrine content of the suprarenal gland [18] have been reported. Microscopic studies of the endocrine glands in these patients gave no evidence of greater damage than other organs, with the exception of the suprarenals, which showed marked hyperemia, small hemorrhages in the medulla, areas of necrosis with indistinct cell outline, and nuclear disintegration.

Nervous System.—The greatest impairment noted in our cases is the deleterious effect on the nervous system. Various changes have been reported (hyperemia of the meninges and brain; also of the subarachnoid spaces, chromatolytic changes, alterations in the glial cells and Golgi apparatus, disintegration of the axis cylinder and medullary sheaths, and partial optic atrophy) [22] but no characteristic involvement has been recognized. Conjunctivitis, retrobulbar neuritis and cataract have been observed in animals and in human beings.[23]

TABLE 2.—*Thallium Content of Viscera of Persons Dying in Fresno Thallotoxicosis Outbreak*

Tissue	Thallium Content: Mg. per Kilogram of Fresh Weight				
	Case 1	Case 3	Case 5	Case 7	Case 8
Kidney	11.6	5.3	4.4	2.7	5.5
Liver	5.5	...	...	3.7	...
Lung	7.7	...	...	3.3	...
Heart	3.6	...	...	...	...
Spleen	2.9	4.6	6.6	...	...
Intestine	...	...	...	3.6	...
Bone	...	...	...	...	Trace

The early involvement of the peripheral nervous system is seen clinically in the pain, tenderness, acroparesthesia, objective sensory disturbances and weakness in the extremities, followed shortly in the severe cases by disturbances of the sensorium, convulsions, cranial nerve palsies and myoclonic or choreiform twitchings; in less rapidly fatal cases by a psychosis characterized by disorientation, marked restlessness, confusion, and finally in mental deterioration.

Histologic studies of the peripheral and central nervous system of our patients developed a basis for this clinical picture in a peripheral neuritis in the axon of the peripheral nerve, shown by the changes with Bielschowsky stain. Profound and extensive changes were found in the central nervous system. The cortical vessels showed engorgement. Various grades of chromatolysis were seen in the neurons, especially those of the pyramidal tract, the third nucleus, the substantia nigra, and the pyramidal cells of the globus pallidus. The vessels were distended with blood and there were localized areas of edema. In a more chronic case there was striking edema of the pia

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15. Kaps.[1]

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18. Buschke and Peiser.[1]

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21. Munch.[1] Buschke and Peiser.[1] Hecke.[13]

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arachnoid. Round cell perivascular infiltration was not a part of the microscopic picture.

In five patients, the last recorded rectal temperatures were 102.8, 106.4, 107, 107.2 and 108.2 F.; in another the temperature by mouth was 104.8 F. It is fairly well accepted that the cells of the tuber cinereum send out impulses having to do with heat regulation. Hemorrhages in the ventricles and pontile hemorrhages cause hyperpyrexia. With the very evident and extensive neuron damage, it seems plausible that the marked hyperpyrexia was due to such an involvement. Other symptoms of thallium intoxication, such as alopecia, salivation, herpetiform lesions on the lips and increased perspiration with a paradoxical reaction to pilocarpine, may be explained by an involvement of the endocrine sympathetic system.

TOXICOLOGY

Samples of the thalgrain responsible for this outbreak were analyzed [24] and found to contain 7 and 7.7 mg. of thallium per kilogram, corresponding to 0.9 per cent of thallium sulphate. Samples of the mixed barley and wheat flour from the Tipton home contained 0.75 per cent of thallium, and a trace was found in the bran. Tortillas obtained from the Selma home had dried out previous to analysis but showed 4.55 mg. of thallium per kilogram. It is estimated that each tortilla would contain approximately from 1.25 to 2.0 mg. of thallous sulphate. Since the exact quantities consumed are unknown, it is not possible to determine the total amount of thallium ingested.

Viscera were collected at necropsy, preserved with formaldehyde, and chemically analyzed for thallium, with the results given in table 2. The presence of thallium was demonstrated in every tissue tested. In making toxicologic studies, it would seem desirable to examine the kidney, liver, lung and spleen.

SUMMARY AND CONCLUSIONS

Grain containing 1 per cent of thallium sulphate was illegally procured, ground and incorporated in tortillas. An unknown amount was consumed by at least thirty-one Mexicans. Symptoms developed in twenty within from one to three days; fourteen were hospitalized, and six died of primary thallotoxicosis within sixteen days. The others survived under treatment, one dying about two months later.

The absorption and action of thallium were rapid in these cases, as indicated by the development of alopecia, even under treatment.

These cases presented a well defined clinical picture of abdominal colic, nausea, vomiting and diarrhea or constipation, stomatitis, alopecia, peripheral neuritis, and symptoms referable to cerebral involvements (ptosis, strabismus, convulsions, myoclonic or choreiform movements and optic atrophy).

From our present study, we would recommend that treatment consist of: (1) emetics; (2) fixation by intravenous injections of sodium iodide; (3) gradual elimination by natural means or by the injection of small doses of sodium thiosulphate with careful attention to the urinary thallium excretion; (4) symptomatic treatment as indicated, and (5) rehabilitation by the administration of fluids, calcium salts, dextrose, orange juice, cod liver oil, and various nutritious foods. If pulmonary congestion is not present, pilocarpine may be administered to stimulate the endocrine system, and salivary and intestinal elimination. In case the administration of sodium thiosulphate causes a sudden exacerbation of thallium intoxication, iodides should be promptly administered and no further attempt should be made to use sodium thiosulphate for this purpose. Further studies are under way with a view to improving this procedure.

Postmortem examinations on seven human beings dying after exposure to thallium showed the following characteristic pathologic picture:

(*a*) Gross Examination: Alopecia, stomatitis, a yellow appearance of the liver showing cloudy swelling, edema and hyperemia of the lungs, and congestion of the leptomeninges.

(*b*) Microscopic Examination: Fatty infiltration and central necrosis of the liver, diffuse nephritis, gastroenteritis, degenerative changes and hemorrhages in the medulla of the suprarenals, pulmonary edema and widespread degenerative changes in the nerve cells and axons.

Chemical analyses revealed the presence of detectable amounts of thallium in the kidneys, liver, lungs and spleen.

24. We wish to acknowledge the assistance of Mr. Justus C. Ward, of the Control Methods Research Laboratory at Denver, in making certain chemical analyses; also of Mr. Paul A. Shaw, of the Hooper Foundation at San Francisco, in permitting the use of his newly developed, unpublished method for the chemical determination of thallium.

THE PHYSIOLOGY OF THE COMMON BILE DUCT

A SINGULAR OBSERVATION

A. C. IVY, M.D.
W. L. VOEGTLIN, B.S.
AND
HARRY GREENGARD, M.S.
CHICAGO

Anatomic evidence [1] indicates that circular muscle fibers surround the duct of Wirsung and the common bile duct individually just before they join the ampulla and may serve as a sphincter for each. However, the fibers are frequently so knit together that it would appear that one could not contract without the other and so occluded both ducts. Burget and Brocklehurst,[2] observing the guinea-pig, report that there is a definite anatomic and physiologic sphincter at the junction of the common bile duct with the ampulla and that, when the ampulla contracts, the sphincter contracts to prevent regurgitation of the bile from the ampulla into the common duct. There is no physiologic evidence indicating the existence of such a sphincter in the dog and in man. However, we have recently made an observation in man which, according to one interpretation, indicates that such a sphincter may exist.

A series of experiments on human subjects was being performed in which secretin, containing some cholecystokinin, was injected intravenously with a duodenal tube in place to determine the pancreatic response. The injection usually promoted in most subjects a copious flow of pancreatic juice and bile. However, in one subject (A. C. I.), the duodenal tube was passed into the duodenum, and after several minutes a flow of bile-stained fluid (0.8 mg. of bilirubin) occurred. Then a

From the Department of Physiology and Pharmacology, Northwestern University Medical School.

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clear fluid not stained with bile was obtained. After a suitable control flow had been obtained, secretin-cholecystokinin (300 dog doses of secretin and 10 dog doses of cholecystokinin) was injected intravenously. A copious flow of a clear to slightly opalescent, strongly alkaline, enzyme-rich fluid was obtained, amounting to 162.5 cc. in forty-nine minutes. Ten minutes after the injection, the subject complained of a gradually increasing pain beneath the ribs in the right hypochondrium and just below the right scapulla—a typical gallbladder distress but not colic. At the end of forty-nine minutes, it was decided to inject some concentrated magnesium sulphate (50 cc. of 33 per cent) into the duodenum to ascertain its effect on the pain and whether bile flow might be caused to resume. The gallbladder distress disappeared in about two minutes after the magnesium sulphate was injected and bile soon began to flow from the duodenal tube. Shortly after (seven minutes), dark bile-stained fluid drained which contained 92.8 mg. of bilirubin.

Obviously, in this subject, something prevented the flow of bile into the duodenum, so that only pancreatic juice was obtained, and the pressure in the biliary passages was sufficient to induce gallbladder distress. The magnesium sulphate must have relaxed some spastic sphincter in the intramural portion of the bile duct, relieving the pain and permitting bile to flow into the duodenum. It is hardly rational to think that some factor inhibited the liver from forming bile for forty-nine minutes, particularly in view of the occurrence of the gallbladder distress.

To explain adequately the observed facts, only two alternatives appear tenable to us; one is that a sphincter (sphincter proprius ductus choledochi) exists in this subject, as in the guinea-pig, at the junction of the common duct with the ampulla which became spastic for some reason and prevented a flow of bile but not of pancreatic juice. The other is that in this subject the duct of Wirsung opens into the duodenum separately from the common bile duct and that a spasm of the sphincter of the common duct (sphincter ductus choledochi) was present. Another possibility which must be considered is that the entire sphincter of Oddi was spastic and that the pancreatic juice obtained in this subject came solely from the accessory pancreatic duct, which sometimes opens independently into the duodenum. This is not likely because the maximum rate of flow in this subject was 5.2 cc. per minute, and the maximum rate of flow observed by us in other experiments in which the pancreatic juice was diluted with bile was 7.5 per minute; that is, we believe that the rate of flow of pancreatic juice was too great to be accounted for as coming from an accessory duct. (It should be mentioned that, eighteen months ago, a cholecystogram, which was made during another experimental study, showed the gallbladder of the subject to be normal and free of stones. Cholecystograms made by Dr. B. H. Orndoff subsequent to the experiment described in this report yielded normal gallbladder results.)

Irrespective of which explanation is accepted, the significant observations are, first, that under rare circumstances one may obtain practically pure pancreatic juice from the duodenum of a normal man; second, that in a normal human subject, gallbladder pain may be experienced in the presence of spastic obstruction of the intramural portion of the common bile duct provided the gallbladder is concurrently excited to contract, and, third, that the spasm and distress may be relieved by magnesium sulphate administered intraduodenally. The second observation, which strongly indicates that distress and pain may be initiated on a functional basis in an apparently normal biliary tract system, we believe, is not only interesting but also clinically significant. Such an observation may explain the complaint of certain patients seen by the clinician in whom mild attacks of gallbladder pain have been experienced and in whom there is no history or evidence of icterus or stones and removal of the gallbladder reveals it to be normal histologically.

303 East Chicago Avenue.

POLYNEURITIS OF PREGNANCY

A DIETARY DEFICIENCY DISORDER

MAURICE B. STRAUSS, M.D.
AND
WILLIAM J. McDONALD, M.D.
BOSTON

It is customary to refer to any and all pathologic conditions developing during pregnancy as manifestations of some occult toxemia, relief from which may be secured by terminating the gravid state. As yet, not one of the "toxins" allegedly responsible for the anemias of pregnancy, for the polyneuritis of pregnancy, for hyperemesis gravidarum, or for eclampsia has been identified, isolated or recovered in any form.

It is not many years since pernicious anemia, pellagra and beriberi were commonly considered disorders due to the action of hypothetic toxins. To this day, in fact, adherents of the toxic theory are still endeavoring to overcome the evidence that these conditions are dietary deficiency diseases either due directly to faulty diet or indirectly arising from some conditioning gastro-intestinal factor.

The anemias of pregnancy have frequently been considered toxic manifestations of the gravid state. Investigations[1] have not only failed to reveal any evidence of toxemia but show that dietary deficiencies, especially of iron, vitamin B_2 and related substances, can account for both the hypochromic and the macrocytic (pernicious) anemias of pregnancy. In some cases, a direct lack of these substances in the diet can be held responsible, but in most instances the deficiency can be explained as due to gastric secretory and related defects. Pregnancy normally produces marked reduction in gastric secretion,[2] and since the fetus is able to drain the maternal organism to supply its needs, the pregnant state is indeed one that readily enhances the development of dietary deficiency disorders. Patients with anemia of pregnancy, if treated on a quantitative basis by supplying the materials that are lacking, recover.

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), and the Obstetrical Service of the Boston City Hospital; the Departments of Medicine and of Tropical Medicine of the Harvard Medical School, and the Department of Obstetrics of the Tufts Medical School.

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Our purpose in this communication is to present evidence which favors the view that the polyneuritis of pregnancy is a deficiency disease and may be satisfactorily treated as such. The condition is one of the less common complications of pregnancy and occurs especially in association with persistent vomiting, as first noted by Whitfield,[3] a condition which, of course, is very favorable for the development of a dietary deficiency disorder. Berkwitz and Lufkin [4] noted that three of their four patients with this disease died, and the fourth survived only after a therapeutic abortion and a stormy course. They have reviewed the literature and collected a total of fifty-two undoubted cases of this disease. Severe "pernicious" vomiting was present in forty of forty-one patients in whom note was made as to this condition. This usually began as "physiologic" vomiting during the first two months of pregnancy and gradually became more severe until it assumed the "pernicious" type. The first neurologic symptoms occurred about the third or fourth month. Weakness, numbness and muscle pain, generally most marked in the legs, predominated. In the early stage the patient, already considered neurotic, because of her hyperemesis, was usually held to suffer from hysteria, since the subjective symptoms were more marked than the slight objective paralysis and anesthesia at that time. As the condition progressed, the paralysis of the legs became pronounced, the arms were involved, and the abdominal and thoracic muscles sometimes were affected. Sphincter disturbances were common. Mental changes not infrequently occurred. Death resulted from exhaustion, intercurrent infection or respiratory paralysis. The only constant physical signs other than the neurologic signs were loss of body weight and tachycardia. Laboratory examinations usually were negative, except for anemia, which was frequently present to a moderate degree. Gastric analyses were not recorded.

Berkwitz and Lufkin summarize their paper as follows: "The clinical and pathological picture of the nerve changes in pregnancy is the same as that resulting from alcoholism, infectious conditions, and diet deficiency disturbances such as beriberi and pellagra . . . the exact nature of the toxins producing neuronitis is still unknown."

Improvement did not occur in their fifty-two collected cases during pregnancy, and even after removal of the fetus an average mortality of 25 per cent is to be expected. In their view that the polyneuritis of pregnancy is a toxemia which should be treated by immediate evacuation of the uterus, they are supported by most observers.

Against this rather hopeless outlook, we present certain facts and observations, indicating the curability of the condition. First, and of most importance, is the fact that severe vomiting almost always occurs recurrently for many weeks before the onset of polyneuritis. This, of course, prevents the patient from ingesting and absorbing the proper food. Secondly, it has been shown [5] that abnormalities of the gastro-intestinal tract can play an important rôle in the causation of deficiency diseases, and in pregnancy there is ordinarily a marked decrease of gastric secretory function.[2] Thirdly, in pregnancy the fetus takes all sorts of materials from the maternal organism, no matter what depletion may result to the mother. Fourthly, the clinical and pathologic examination in polyneuritis of pregnancy is identical with that of beriberi and alcoholic polyneuritis and is unlike the more strictly motor nerve involvement due to lead, and triorthocresyl phosphate (jamaica ginger) polyneuritis. The concept that certain sorts of polyneuritis often attributed to particular conditions or diseases may be particularly due to lack of vitamin B has been suggested by other investigators, and observations pertaining to this aspect of alcoholic neuritis and other sorts of neuritis have been pursued in this clinic for several years.

With these facts in mind, we present the following case reports:

CASE 1.—A white woman, aged 32, married, admitted Dec. 4, 1928, had been perfectly well until August, 1928. At that time, in the fourth month of her first pregnancy, she began to vomit. This steadily increased in frequency and severity. In September she entered another hospital, where she remained for five weeks, being treated by rectal infusions but continuing to vomit almost everything taken by mouth. Late in October she was admitted to the Boston Lying-In Hospital, where, after all treatment had failed to stop the vomiting, cesarean section was performed and a dead fetus removed. Vomiting ceased at once.

A fortnight after operation, numbness and tingling were noticed in the hands and legs. When she attempted to stand, she found that her legs would not support her. Two weeks later she was transferred to this hospital, her weakness having increased in severity in that time.

The family and past histories were irrelevant. Physical examination was essentially normal except as noted later. The pulse rate was from 80 to 100 per minute. Neurologic examination revealed moderate weakness of the upper extremities and complete paralysis of the legs from the knees down. Coordination was fair in the finger-nose test. Weakness prevented testing the coordination in the legs. The deep reflexes in the arms were diminished, and all tendon reflexes in the legs were absent. Plantar stimulation evoked no response. Skin sensation was markedly diminished over both legs and moderately diminished over the arms. Vibratory sensation was absent in the legs and normal in the arms. Position sense was diminished in both hands and feet, more so in the latter. The calf muscles and nerves were extremely tender to pressure.

Laboratory studies were as follows: red blood cells, 3,140,000 per cubic millimeter; hemoglobin, 55 per cent (Sahli); white blood cells, 6,800 per cubic millimeter. The red blood cells showed moderate variation in size and shape and macrocytosis. Slight achromia was also present. A differential count of the leukocytes showed: polymorphonuclear neutrophils, 74 per cent; eosinophils, 2 per cent; lymphocytes, 6 per cent; monocytes, 17 per cent; metamyelocytes, 1 per cent. The Kahn reaction for syphilis was negative. Nonprotein nitrogen of the blood was 35 mg. per hundred cubic centimeters. Blood sugar (fasting) was 104 mg. per hundred cubic centimeters.

Gastric analysis with an alcohol test meal showed no secretion of free hydrochloric acid.

The urine showed a faint trace of albumin and occasional hyaline casts and leukocytes. Excretion of phenolsulphonphthalein was 35 per cent in two hours. A Mosenthal test of urine concentration was normal.

Lumbar puncture revealed a clear, colorless fluid under no increased pressure. The total protein was 42 mg. per hundred cubic centimeters. The Wassermann reaction was negative. The colloidal gold curve was 0000000000. Roentgenograms of the skull showed it to be normal.

The patient was placed on a high protein diet at once. No other treatment was given. Improvement was slow but steady, and on discharge, March 4, 1929, the patient was able to walk alone without difficulty. The erythrocytes were then 4,000,000

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per cubic millimeter, hemoglobin 70 per cent, leukocytes 9,500 per cubic millimeter. Slight achromia of the red blood cells persisted, but they were normal in size and shape.

This patient presented the classic picture of multiple neuritis. The onset occurred after the therapeutic termination of pregnancy in a woman who had vomited for at least three months prior to this. The patient had gastric anacidity and an anemia of the macrocytic and hypochromic type, which can be associated with deficiencies of both vitamin B_2 and iron. Improvement was slow but steady on a high protein diet; i. e., one rich in vitamin B and iron. However, the only fact that might serve as a control of this therapy was her unfavorable course of a month prior to its institution, so that no conclusions may safely be drawn.

CASE 2.—A white woman, aged 30, married, entered the hospital, Jan. 10, 1929. One month before, when she was two months pregnant, she commenced to have morning nausea. This grew increasingly more severe until after a week she developed an acute infection of the upper respiratory tract and commenced to vomit more or less constantly. At that time moderate pin-and-needle sensations were present in her arms. The uterus was enlarged to the size of a three months pregnancy. Physical examination was otherwise normal. The family and past histories were irrelevant. Neurologic examination was entirely normal. Laboratory studies showed: red blood cells, 4,790,000 per cubic millimeter; hemoglobin, 95 per cent (Sahli); white blood cells, 7,600 per cubic millimeter. The icteric index was 10. Stained blood films showed no abnormalities. The Kahn reaction for syphilis was negative. The nonprotein nitrogen of the blood was 32 mg. per hundred cubic centimeters. The urine showed a slight trace of albumin and a few leukocytes and granular casts. The excretion of phenolsulphonphthalein was 25 per cent in two hours.

The patient was given nothing by mouth but was fed by rectal infusions. Two weeks after admission, she was discharged, vomiting having completely ceased.

During the next four weeks she remained in bed at home, eating very little. Her memory became poor and she was confused. For two days before readmission she had had a slight bloody vaginal discharge. Physical examination at this time was recorded as normal. The uterus was felt just below the umbilicus. Fetal heart sounds could not be heard. Details of the neurologic examination at this time are not available, but a competent neurologist recorded his opinion that the patient had multiple neuritis and a toxic psychosis.

Laboratory examination showed: red blood cells, 3,510,000 per cubic millimeter; hemoglobin, 70 per cent (Sahli); white blood cells, 13,050 per cubic millimeter. The differential count was: polymorphonuclear neutrophils, 67 per cent; eosinophils, 1 per cent; lymphocytes, 29 per cent; monocytes, 3 per cent. The nonprotein nitrogen of the blood was 37 mg. per hundred cubic centimeters. The urine showed a slight trace of albumin, and hyaline and granular casts. The phenolsulphonphthalein excretion was 40 per cent in two hours. Lumbar puncture revealed a clear, colorless fluid under normal pressure. The total protein was 45 mg. per hundred cubic centimeters. The colloidal gold curve was 1111100000. The Wassermann reaction was negative.

On the sixth day in the hospital (February 23) the patient miscarried a macerated fetus. Under gas-oxygen anesthesia the uterine cavity was subsequently curetted. Shortly thereafter, in spite of the moderate neuritis and psychosis, the patient's family insisted on taking her home.

Two months later, April 27, the patient was readmitted, totally unable to walk, with marked mental confusion and loss of memory. Emotional instability was also present. Physical examination revealed evidence of marked loss of weight. The pulse rate ranged from 100 to 120. Neurologic examination showed some weakness of the arms and paralysis of the legs with atrophy of the muscles and tenderness of the calves on pressure. Tendon reflexes were abolished in the legs and diminished in the arms. Plantar stimulation gave no response. Although paresthesias were present in the hands, no objective change in skin sensation was made out. Vibratory and position sense were diminished in the legs but normal in the arms. Nystagmoid jerks were observed in both eyes, and a tremor of the tongue was noted.

Laboratory examinations showed: red blood cells, 4,120,000 per cubic millimeter; hemoglobin, 70 per cent (Sahli); white blood cells, 8,550 per cubic millimeter. The differential count was: polymorphonuclear neutrophils, 76 per cent; lymphocytes, 19 per cent; monocytes, 5 per cent. Moderate achromia with variation in size and shape of the erythrocytes with some microcytosis was present. The urine was entirely normal. Blood and spinal fluid Wassermann reactions were negative. The spinal fluid was essentially as previously noted. Gastric analysis showed 20 cc. of tenth normal free hydrochloric acid twenty minutes after the administration of 50 cc. of 7 per cent ethyl alcohol in water. No free acid was present in specimens removed forty and sixty minutes later.

Shortly after this admission, the patient was given a high vitamin diet (including orange juice, 100 Gm. of raw liver and six yeast vitamin [Harris] tablets daily) and 6 Gm. of iron and ammonium citrate daily. Improvement commenced a few weeks after the diet was begun, and she left the hospital, June 17, able to walk, with slight assistance.

This patient presented a clear picture of multiple neuritis with its onset about the fifth month of pregnancy, following several months of vomiting and anorexia. During a period of two months without therapy, following a miscarriage, the patient grew steadily worse. Laboratory examinations showed moderate anemia and gastric hypo-acidity. Improvement commenced shortly after the administration of iron and a diet rich in vitamins. A so-called toxic psychosis of a type associated with this sort of polyneuritis also cleared under this dietary regimen.

CASE 3.—A white woman, aged 40 years, married and pregnant, first developed symptoms of polyneuritis, May 13, 1932. The family history was irrelevant. The past history was of interest, as seven years previously the patient had been seen in a fulminating eclamptic toxemia, which had developed with great suddenness in the last month of her first pregnancy. At this time she had had two convulsions; the blood pressure was 170 systolic and 100 diastolic, and the urine contained large amounts of albumin and occasional casts. Labor was induced and a 4 pound 12 ounce (2,155 Gm.) macerated fetus was delivered. Convalescence was uneventful. A month later the urine was normal, and blood pressure was 115 systolic and 80 diastolic.

In August, 1930, she was seen in the second month of her second pregnancy. Nausea and vomiting were considerable, but the urine and blood pressure were normal. Three months later, the nausea and vomiting had completely ceased but a faint trace of albumin was present in the urine. This was not again observed during the next two months, but on Feb. 4, 1931, the blood pressure had risen to 140 systolic and 80 diastolic, and albuminuria was present, together with edema of both legs. During the next three weeks fetal movements ceased, fetal heart sounds could no longer be heard, the blood pressure remained elevated and albumin persisted in the urine. February 27, the patient was delivered of a 4 pound (1,810 Gm.) macerated fetus. The placenta was small and markedly infarcted. Convalescence was uneventful, the blood pressure and urine becoming normal.

Feb. 5, 1932, the patient presented herself in the second month of a third pregnancy with moderate anorexia. Examination was otherwise normal. During the next two months increasing vomiting occurred, until the patient was able to retain nothing by mouth. She was admitted to another hospital and given dextrose and saline solution by subpectoral and intravenous injection, together with rectal infusions. Slight albuminuria was present. In a week she went home, able to retain her food fairly well. During April she vomited a few times a week and had slight albuminuria and a slowly rising pulse rate. Early in May vomiting ceased, but numbness and tingling of the hands and feet developed. The pulse rate was

104 per minute. Within two weeks difficulty in walking was experienced; the patient became irritable and forgetful. Albumin was no longer present in the urine. Early in June the pulse rate had risen to 116; the patient was unable to stand, and paresthesias were marked. June 5, the neurologic examination recorded in the accompanying table was typical of a severe polyneuritis. At that time the patient had a macrocytic and hypochromic anemia. Red blood cells numbered 2,870,000 per cubic millimeter; hemoglobin was 51 per cent (Sahli); white blood cells numbered 2,750 per cubic millimeter; and the mean corpuscular volume was 100.3 cubic microns, the mean corpuscular hemoglobin concentration, 27.6 per cent, and the icteric index, 2. The Wassermann and Hinton reactions of the blood were negative. The urine was normal. The blood pressure was 104 systolic and 60 diastolic. Therapy was immediately instituted with 6 Gm. of iron and ammonium citrate, 12 Gm. of autolyzed yeast (vitamins B_1 and B_2), and 12 cc. of cod liver oil daily. No changes were made in the general diet. Within ten days, improvement was noted by the patient. The objective changes in the neurologic status of the patient are given in the table. Five weeks after the institution of therapy, the patient was considerably improved, but, a certain amount of gastro-intestinal distress having developed, the dose of iron was halved. Shortly afterward liver extract No. 343

Neurologic Examinations During and After Pregnancy (Case 3)

	June 5	June 23	July 9	July 29	Sept. 2	Oct. 29	Dec. 15
Motor system:							
Weakness:							
Arms	****	**	*	*	N	N	N
Hands	**	**	*	*	N	N	N
Legs	****	***	**	**	**	**	N
Feet	***	**	*	*	N	N	N
Muscle tone:							
Calves	****	****	***	**	*	N	N
Muscle tenderness:							
Calves	****	***	**	*	*	N	N
Reflexes:							
Both biceps, triceps	*	*	N	N	N	N	N
Right knee jerk	****	****	****	***	**	**	**
Left knee jerk	****	****	****	****	***	**	**
Both ankle jerks	****	****	****	****	****	****	** *
Both plantars	*	*	N	N	N	N	N
Incoordination:							
Both legs	****	****	**	N	N	N	N
Sensation:							
Pin and brush:							
Both arms	N	N	N	N	N	N	N
Right leg	***	**	N	N	N	N	N
Left leg	***	**	*	*	N	N	N
Position:							
Both arms	*	*	*	N	N	N	N
Right foot	****	****	**	*	N	N	N
Left foot	****	****	***	**	N	N	N
Vibration:							
Both arms	*	*	*	N	N	N	N
Right tibia	***	*	*	N	N	N	N
Left tibia	***	*	*	*	N	N	N

N indicates normal function. The number of stars (*) indicates the extent of the deviation from normal. September 28, the patient was delivered by cesarean section of a healthy full-term infant. Treatment with autolyzed yeast (12 Gm.) and iron and ammonium citrate (6 Gm.) daily was commenced June 6.

(N. N. R.) rich in vitamin B_2, derived from 600 Gm. of liver, and twelve yeast vitamin (Harris) tablets (chiefly vitamin B_1), were prescribed daily in place of the autolyzed yeast.

This change was made with the thought that liver extract might contain, in addition to its vitamin B_2 content, some product such as the material potent in pernicious anemia which might be of benefit. In order to continue a high vitamin B_1 intake, the concentrated tablets derived from yeast were employed.

Improvement continued in both the general health and the neurologic condition of the patient, as recorded in the table. No attempts at massage or exercises were employed. September 28, the patient was delivered of a healthy baby girl by cesarean section. Iron, liver extract and yeast concentrate therapy was omitted for a week, and 12 Gm. of autolyzed yeast daily was administered. A decline in the blood count during the next fortnight made it necessary to recommence the administration of iron also.

As soon as the patient had recovered from the laparotomy, massage and exercise were employed. In addition to subjective improvement, continued regression of abnormal neurologic signs occurred, as recorded in the table.

December 15, the blood was essentially normal. The patient was able to do her own housework. The only residuals of the polyneuritis were a diminution of the knee jerks and absent ankle jerks.

This patient suffered from typical polyneuritis of pregnancy with a macrocytic and hypochromic anemia, the onset following a prolonged period of vomiting. Her unfavorable course was rapid and marked before the initiation of vitamin therapy. The rising pulse rate was not unlike that seen in beriberi. Improvement in the nerve state and blood occurred within ten days of the commencement of treatment and continued throughout the remaining three months of pregnancy. At term, there were only a few abnormal neurologic conditions. The patient was delivered of a healthy baby and was able to walk without difficulty shortly thereafter. Absent ankle jerks and diminished knee jerks were the only residual manifestations at that time.

COMMENT

It seems probable from these observations that the polyneuritis of pregnancy is not a toxemia but a dietary deficiency disorder, similar to the polyneuritis of beriberi, which is known to be due to vitamin B_1 deficiency. It is known that in regions where beriberi is endemic (that is, where deficient diets are partaken by many individuals in the community), the disease frequently occurs in pregnant women.[6] In regions where beriberi is not endemic, the deficiency may be brought about solely by the restriction in the food intake and absorption induced by hyperemesis, or there may be, in addition, conditioning gastro-intestinal factors, such as occur in the anemias of pregnancy. The fetal demand is an added drain on the maternal organism.

In view of this, rational therapy should avoid operative intervention with pregnancy and be directed to supplying suitable material to meet the deficiency. In cases in which suitable material cannot be retained by the stomach, the use of intramuscular therapy seems indicated.

Since it has been observed that certain cases of macrocytic (pernicious) anemia of pregnancy lack not merely a dietary factor associated with vitamin B_2 but also an unidentified factor like the one absent in addisonian pernicious anemia and which is present in normal human gastric juice, it is possible that a similar dual mechanism may be at work in certain cases of polyneuritis of pregnancy. For this reason the use of liver and liver extracts, both by mouth and by injection, should be carried out in cases not responding to simple preparations of vitamins B_1 and B_2.

Only when a sufficient number of these cases have been treated along the lines indicated can definite conclusions be drawn. The rarity of the condition precludes systematic study in any one clinic except during a period of many years. Prophylactic use of vitamin B in all patients with "pernicious" vomiting seems indicated.

CONCLUSIONS

1. The polyneuritis of pregnancy is probably a dietary deficiency disorder similar to beriberi.

2. Rational therapy should aim to supply the deficiency, which may be especially some portion of the vitamin B complex; large amounts of concentrates of this substance are advised.

3. In "pernicious" vomiting of pregnancy, prophylactic use of vitamin B is suggested.

6. Hofmann, J. A.: Beriberi in Chinese Women and Its Relation to Childbearing, China M. J. **38**: 987 (Dec.) 1924.

THE COLOR OF THE NASAL SEPTUM

A CRITICAL STUDY OF ITS SUPPOSED VALUE AS AN INDEX FOR DIETARY THERAPY IN DISEASES OF THE UPPER RESPIRATORY TRACT

L. B. BERNHEIMER, M.D.
AND
DAVID J. COHN, PH.D.
CHICAGO

In recent years the belief has been voiced by Jarvis and others that respiratory symptoms and pathologic changes in the respiratory system are brought about by faulty acid-base metabolism. Jarvis and his group have expressed the opinion that the color of the mucous membrane of the nasal septum is an index of the acid-base balance in the body: pale septums being present in states of alkalosis, red septums in acidosis. The group of patients with pale septums, according to Jarvis,[1] show a history of having eaten excessive amounts of foods producing alkaline ash and are susceptible to hay fever, asthma, hyperesthetic rhinitis, coryza and bronchial infection, whereas the patients with red septums give a history of having eaten excessive amounts of acid-producing foods and suffer from anorexia, lassitude, emotional instability, irritability, constipation, dry skin, insomnia, fatigue and repeated infections.

The treatment that Jarvis and his group propose for both these types of patients is mainly dietary. The patients with the so-called pale nasal septum complex, that is to say, those supposedly suffering from alkalosis, are placed on diets high in acid-producing foods, such as the proteins. This treatment is supplemented with small doses of dilute nitrohydrochloric acid. Patients with the "red septum symptom complex," that is, those considered to be suffering from acidosis, are given diets containing large amounts of fruits and vegetables (foods producing alkaline ash) and also small doses of sodium bicarbonate. Excellent clinical results have been reported with these dietary treatments by Jarvis and others in pansinusitis, polypoidal nasal disease, hay fever, hyperesthetic rhinitis and asthma, as well as the constitutional symptoms presenting themselves in the "red septum symptom complex."

Unfortunately, in the reports by Jarvis and his co-workers, the diagnosis of acidosis or alkalosis rests entirely on the color of the mucosa of the nasal septum. There is no evidence of either a clinical or a laboratory nature to show whether the patients treated had an abnormal acid-base balance to begin with or whether the acid-base balance was in any way affected by the treatment.

The present work was undertaken to investigate the rationale both of the method of diagnosis by means of the color of the nasal septal membrane and of the suggested dietary treatment. For this purpose, a series of patients and of normal controls were studied to determine (1) whether an abnormally red or pale color of the nasal septal mucous membrane actually indicates a state of acidosis or of alkalosis in the subject, and whether this color changes with diet and progress of disease; (2) whether patients suffering from various diseases of the respiratory tract are benefited by alkalinizing or acid-producing diets, other factors remaining unchanged.

Read before the American Triological Society, Jan. 9, 1933.
From the Department of Otolaryngology and the Department of Chemistry (Nelson Morris Memorial Institute), Michael Reese Hospital.
1. Jarvis, D. C.: Group Letters.

EVALUATION OF THE COLOR OF THE MUCOUS MEMBRANE OF THE NASAL SEPTUM AS AN AID IN DIAGNOSIS OF DISTURBANCE IN ACID-BASE EQUILIBRIUM

In an effort to determine the relationship between the color of the septal mucous membrane and the acid-base balance of the body, a study was made of a group of fifty patients with clinical signs and symptoms of acid-base disturbance. Among these were seven in diabetic coma, four in the terminal stages of nephritis, three in postoperative shock, three with renal complications of pregnancy and impending eclampsia, twenty-one with severe toxemias due to purulent processes such as osteomyelitis, mastoiditis, acute sinusitis and empyema of the pleural cavity, eleven with bronchopneumonia of the so-called influenzal type with almost overwhelming toxemias, and one with scarlet fever. Each one of these fifty individuals showed the classic clinical symptoms of acidosis; that is, dehydration and hyperpnea, and acetonuria. The color of the septal mucous membrane in thirty-four of these patients (68 per cent) was found to be a normal pink, seven (14 per cent) had distinctly pale septal membranes, and in only nine (18 per cent) were the membranes redder than normal. The seven patients in diabetic coma were treated with insulin, and six recovered. Close daily observation of the nasal mucous membranes during convalescence did not reveal gross alterations in color corresponding to the reestablishment of normal metabolic conditions. In this series of fifty cases, therefore, no relationship could be demonstrated between the color of the septal mucous membrane and the clinical symptoms of acidosis.

On the other hand, all three types of nasal septum were found in a group of 100 clinically normal, healthy men and women. Fifty-four were found to have normal color of the nasal mucosa, twenty-eight had membranes paler than normal, and in eighteen the nasal mucosa was scarlet red. It will be noted that the distribution of the three types of nasal septums is about the same in the group of normal controls as in the patients, excepting that there seem to be fewer patients with the normal pink septums, and more with the pale septums in the normal group.

For the sake of this preliminary study, the hydrogen ion concentration of the blood was used as a criterion of any gross abnormality in acid-base equilibrium in twenty cases. It is to be remembered, however, that the constancy of the hydrogen ion concentration of the blood is very well guarded, both by chemical and by physiologic buffer mechanisms, and that cases of compensated acidosis or alkalosis occur in which the anion and cation balance in the blood is shifted, but the hydrogen ion concentration remains within normal limits (p_H from 7.35 to 7.45). In all twenty patients, despite the clinical signs, the hydrogen ion concentration was within normal limits at the time of examination, yet all three types of nasal mucous membrane color were found present.

These results corroborated the conclusions reached by Feinberg,[2] who determined the p_H on a similar group of individuals.

A more complete study is in progress to determine not only the hydrogen ion concentration but also the alkali tolerance and carbon dioxide combining power in a series of patients in whom the nasal septal color is being followed.

2. Feinberg, S.: Laryngoscope, October, 1932.

An effort to analyze the reasons for the differences in the color of the nasal mucosa in healthy subjects as well as in patients led to the following observations:

1. Atmospheric conditions affect the color of this membrane. Persons exposed to cold, especially in the presence of wind, usually develop red nasal mucous membranes. The same individuals have normal pink membranes under milder weather conditions.

2. Age influences the color of the nasal mucosa of normal individuals. After 60 the membranes tend to become atrophied and are very pale, while the membranes of infants are very red.

Hydrogen Ion Concentration of Blood in Twenty Patients

Patient	Clinical History	Color of Nasal Mucosa	p_H of Blood Serum
1	Hyperesthetic rhinitis with usual complaints of sneezing, nasal block and watery discharge; duration two years	Pale, waterlogged	7.44
2	Hyperesthetic rhinitis; usual complaints as above; duration seventeen months	Pale, waterlogged	7.41
3	Hyperesthetic rhinitis; usual complaints as above; duration three years	Pale, waterlogged	7.41
4	Hyperesthetic rhinitis; usual complaints as above; duration eighteen months	Pale, waterlogged	7.46
5	Hyperesthetic rhinitis; usual complaints as above; duration two months	Pale, waterlogged	7.44
6	Hyperesthetic rhinitis; usual complaints as above; duration nine months	Pale, waterlogged	7.45
7	Hyperesthetic rhinitis; usual complaints as above; duration seven months	Pale, waterlogged	7.45
8	Acute sinusitis; duration ten days	Pale	7.38
9	Chronic right otitis media with cholestoma; duration seven years.	Pale	7.38
10	Seasonal hay fever with pollen asthma	Pale, waterlogged	7.41
11	Seasonal hay fever	Pale, waterlogged	7.41
12	Bronchial asthma; duration four years	Pale	7.40
13	Polypoidal sinus disease; duration three years	Scarlet red	7.44
14	Postthyroidectomy; duration two months	Normal	7.37
15	Acute pharyngitis with cervical adenopathy; duration three days.	Scarlet red	7.38
16	Chronic right otitis media; red septum symptom complex; duration two years	Scarlet red	7.45
17	Secondary laryngitis; red septum symptom complex; arteriosclerosis and hypertension	Scarlet red	7.48
18	Chronic right otitis media; red septum symptom complex; duration ten years	Scarlet red	7.48
19	Frequent attacks of sinusitis; red septum symptom complex; duration two years	Scarlet red	7.45
20	Subacute ethmoiditis; red septum symptom complex; duration one year	Scarlet red	7.41

3. Blonds with pale fair skin have pale mucous membranes, while brunettes with high color have membranes that tend to be red.

4. Posture, exercise, the use of alcohol, the inhalation of dry air or irritants such as dust influence the color of the nasal mucosa.

5. The nine patients with red nasal mucosa, listed under the head of patients giving clinical symptoms of acidosis, were patients with high temperatures at the time of examination. The resultant surface capillary dilatation caused a flushed face and an engorgement of all the mucous membranes of the head and neck and was therefore sufficient to explain the red color of the nasal mucous membrane.

From these observations, it may be concluded that the color of the nasal mucosa varies not only in persons who are ill but also in healthy individuals and that the reasons for these variations are not necessarily of a pathologic nature.

EVALUATION OF THE DIETARY TREATMENT

Except in prolonged starvation, or in complete carbohydrate deprivation, diet is not known to have any very marked effect on acid-base equilibrium. It is true that some foods, such as the proteins, produce acid ash products; others, mainly vegetables and fruits, produce an alkaline ash. However, excepting in cases of severe metabolic disturbances, such as diabetes,[3] nephritis, continued vomiting or diarrhea, the preferential excretion of acid or basic elements by the kidneys, lungs, skin and intestine keeps the hydrogen ion concentration of the blood and tissues in adjustment. The urine may become either acid or alkaline, depending on the diet. Yet the internal acid-base balance is unappreciably affected.[4] Hasselbach found that changing from a high carbohydrate to a high protein diet caused the carbon dioxide capacity of the blood to drop only 3 volumes per cent, which is within normal variations.

Mineral acids and salts do have an effect on the acid-base balance, but fairly large amounts must be administered. Thus, Peters and Van Slyke[5] have shown that 0.026 Gm. of sodium bicarbonate per kilogram (1.5 Gm. for an average individual weighing 60 Kg.) is needed to raise the plasma carbon dioxide 1 volume per cent. It takes 45 Gm. of sodium bicarbonate daily to render the urine continuously alkaline.[6] Therefore, the amount of alkali and acid prescribed in the treatment (e. g., 0.7 Gm. of sodium bicarbonate three times a day) can hardly be expected to exert any influence on the acid-base balance of the patient.

With these theoretical considerations in mind, we studied the actual influence of diet on the course of the disease in question and the color of the septal mucosa in patients suffering with allergic nasal disturbances or asthma. Ten individuals with hyperesthetic rhinitis, five with asthma, six with seasonal hay fever, and three with nasal polyps and an allergic background, were given acid ash diets, with dilute nitrohydrochloric acid as a drug adjunct. This therapy was rigorously pushed over periods varying from three months to one year. No individual in this series responded favorably to the treatment, nor was the color of the nasal mucosa influenced.

Fifteen other individuals were chosen for study who happened to combine scarlet red septums and the symptoms described as being part of the red septum complex. These were given diets producing alkaline ash and, in addition, sodium bicarbonate and Spintrate.[7] These individuals were under observation for five months. Six of them had chronic suppurative sinus disease, two had chronic tracheobronchitis and seven complained of malaise, insomnia, lack of appetite and emotional instability. The prescribed diet failed to influence the color of the nasal mucosa of the fifteen individuals to any extent. The eight patients with a chronic infection of the upper respiratory tract showed no beneficial effects from the diets. Three with subjective symptoms seemed to be benefited, but definite

3. Bock, A. V.; Field, H., Jr., and Adair, G. S.: Acid-Base Equilibrium in Diabetic Coma, J. Metab. Research **1**: 27 (July-Aug.) 1923. Myers, V. C., and Boother, L. E.: Some Variations in the Acid-Base Balance of the Blood in Disease, J. Biol. Chem. **59**: 699 (April) 1924.

4. Blatherwick, N. R.: The Specific Rôle of Foods in Relation to the Composition of the Urine, Arch. Int. Med. **14**: 409 (Sept.) 1914.

5. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company.

6. Haldane, J. B. S.: Experimental and Therapeutic Alterations of Human Tissue Alkalinity, Lancet **1**: 537 (March 15) 1924; The Production of Acidosis, J. Biochem. **19**: 249, 1925. Haldane, J. B. S.; Hill, R., and Luck, J. M.: Calcium Chloride Acidosis, J. Physiol. **57**: 301 (June) 1923. Haldane, J. B. S.: Experiments on the Regulation of the Blood Alakalinity, ibid. **55**: 265 (Aug.) 1931.

7. A dried spinach made by the Spinach Products Company of South Carolina.

conclusions as to the value of the treatment in the alleviation of these symptoms could not be drawn, as one patient felt better immediately after a financial situation in which he was very much concerned had cleared up; one felt better only after a two weeks vacation in the north woods, and one after he had begun systematic daily exercise.

CONCLUSIONS

1. No correlation could be found between the color of the nasal mucosa and the clinical symptoms of acidosis in fifty critically ill patients, all of whom showed clinical symptoms of acidosis with hyperpnea, dehydration and acetonuria.

2. In 100 normal subjects and in twenty patients with various diseases but with normal hydrogen ion concentration of the blood there were found all three types of septal mucosa—pale, normal pink and scarlet red.

3. The color of the nasal septal mucosa was found to be influenced by age, atmospheric condition, type of complexion and other nonpathologic conditions, as well as by alcoholism and body temperature.

4. The use of diets high in foods producing alkaline or acid metabolic products together with the adjunct acid or alkaline drug treatment failed to influence the symptoms or conditions either in a group of patients suffering from allergic nasal or respiratory disease or in a group with malaise or insomnia. In neither group did the diet affect the color of the mucosa of the nasal septum.

104 South Michigan Avenue.

THE FETISH OF TRIPLY DISTILLED WATER

WILLIAM J. ELSER, M.D.
AND
RALPH G. STILLMAN, M.D.
NEW YORK

In a recent article discussing the means of preventing the occurrence of chills following the transfusion of citrated blood, Lewisohn and Rosenthal[1] in their conclusions said: "The use of solutions prepared with triple distilled water is indispensable." This advice has become traditional in our literature since the time when it was first introduced in an attempt to avoid the reactions that followed the intravenous administration of arsphenamine, apparently on the theory that, if one distillation is good, three distillations must of necessity be three times as good. The question, however, appears not to have been subjected to critical analysis.

In the ordinary practice of redistillation, distilled water is taken from a still of the Stokes, Barnstead or similar design and distilled again in a glass apparatus, usually made of pyrex glass but sometimes made of quartz, in which there is a tight connection, sometimes glass to glass, between the flask and the condenser. The distillate is collected in a glass or quartz container. The apparatus, as generally used, is not provided with any device to prevent carrying over of spray from the flask into the distillate, and there is no arrangement for the escape of volatile impurities. If the original distilling apparatus is in good condition and is properly operated, it is unlikely that redistillation as just described will remove from the water anything not removed in the first procedure. A higher grade of water can be produced by the use of an apparatus properly fitted with baffle plates to prevent spray being carried over, and so arranged that it is distilled from acid and alkali permanganate. Such an apparatus is preferably made of quartz and has a relatively small output. It is rarely found to have been used in the preparation of water for making solutions for intravenous administration. We have used such an apparatus for thirty years for the production of triply distilled water, which we have employed in certain serologic tests. In purity, the product of this still approaches what is known as "conductivity water."

The question of reactions following intravenous medication did not assume importance until the introduction of arsphenamine. Prior to that time, practically the only fluid that was introduced directly into the circulation was physiologic solution of sodium chloride, and reactions rarely followed its use. Soon after the introduction of arsphenamine, Wechselmann,[2] stated that distilled water developed something on standing that seemed to be a factor in the production of febrile reactions and recommended the use of freshly distilled water for making up the solutions. His advice was not generally taken, however, until the work of Seibert[3] appeared. She showed that distilled water was likely to become infected on standing and that a gram-negative, thin, motile and non-spore-forming bacillus could be recovered from waters that caused fever when injected intravenously into animals. She pointed out that if the water was sterilized within twenty-four hours after its distillation it was not pyrogenic and did not become so if its sterility was maintained. After her work appeared, much greater emphasis was laid on the need for using freshly distilled water in making solutions that are to be introduced directly into the circulation.

Our experience is entirely in agreement with this idea that the majority of reactions can be avoided by the use of freshly distilled water. At the New York Hospital, the laboratory division took over the manufacture of 50 per cent dextrose solution and the supervision of the production of physiologic solution of sodium chloride, April 1, 1928. Between that date and July 1, 1932, there were issued 10,867 flasks, each containing 100 cc. of 50 per cent dextrose, and it is estimated that at least from 15,000 to 20,000 liters of physiologic solution of sodium chloride was given out. Probably one half of this was administered intravenously. During this period there occurred but one reaction following the intravenous administration of saline solution and in that instance it was found that the solution had been given at too low a temperature. Occasionally, reactions would be reported following the injection of dextrose solution but in no instance could this be attributed to the solution itself, except for one lot in the preparation of which infusorial earth had been used in an experimental modification of the method of preparation. In the other instances, after investigation of the circumstances, it was concluded that the reactions had been due to too rapid

From the Central Laboratories and the Department of Applied Pathology and Bacteriology of the New York Hospital-Cornell Medical College Association.

1. Lewisohn, Richard, and Rosenthal, Nathan: Prevention of Chills Following Transfusion of Citrated Blood, J. A. M. A. **100:** 466 (Feb. 18) 1933.

2. Wechselmann: Neuere Erfahrungen über intravenöse Salvarsaninjektionen ohne Reaktionsverscheinungen, , München. med. Wchnschr. **58:** 1510, 1911.

3. Seibert, Florence B.: Fever-Producing Substance Found in Some Distilled Waters, Am. J. Physiol. **67:** 90 (Dec. 1) 1923.

injection or, on two occasions, to a condition of increased reactivity on the part of the patient. It must be borne in mind that these injections were given by the intern staff and that it was exceedingly difficult to control the rate of injection in all cases. These solutions were made with distilled water, distilled once with a Barnstead still and always sterilized on the same day that the water was distilled. The raw water was New York City tap water, which is generally regarded to be of a high degree of purity. It is all chlorinated but does not contain free chlorine at the tap.

The experience of Dr. Bernheim in the laboratory of the New York Hospital lends additional support to our position. She [4] found that, in the use of 2 per cent sodium citrate solution for intravenous administration, the severity of the reactions that followed were directly proportional to the time elapsing between the distillation of the water and the sterilization of the solution. If this period was less than twenty-four hours, no reaction occurred; if it was between twenty-four and forty-eight hours, a certain proportion of the patients had mild chills, while, if the period was more than forty-eight hours, a large percentage of the patients suffered severe chills.

It is significant that in a fairly large (300 bed) hospital over a period of four years and three months there occurred only a single reaction following the intravenous infusion of physiologic solution of sodium chloride prepared with singly distilled water, the one reaction being due to the injection of a cold solution. It seems impossible that this could occur if water that had undergone but a single distillation contained any appreciable amount of pyrogenic substance. What is much more likely is that reactions that follow the use of other solutions are due to other causes.

A number of factors have been accused of being the real cause for the reactions. The presence of undissolved particles may sometimes be at fault and the p_H of the solution may occasionally, though probably rarely, be blamed. During the past few years, however, more and more emphasis has been placed on the importance of the slow introduction of solutions into the veins, especially when these solutions are hypertonic. Levy,[5] Titus and Dodds,[6] Palmer, Turner and Gibb,[7] Randall,[8] Ravdin,[9] Huffman,[10] Hendon,[11] Hirschfeld, Hyman and Wanger [12] and Hyman and Hirschfeld [13] have successively called attention to the need of introducing such solutions with great deliberation, and while they do not altogether agree on the absolute speed which is recommended and which appears to differ somewhat with solutions of different substances, the trend seems to be toward advising a speed not to exceed 3 to 5 cc. per minute. This is startlingly substantiated by the more recent report of Hyman and Hirschfeld in which they show that almost anything can be introduced into the veins of a patient provided it is done slowly enough.[14] They maintain that even an antigen may be injected intravenously into a sensitized animal without the production of anaphylactic shock, provided it is done sufficiently slowly. Under the circumstances, the excellent results reported by Lewisohn and Rosenthal [1] are due much more probably to the slow speed of the injection than to the use of triply distilled water or the attempt to eliminate completely foreign protein from the solutions used.

Naturally, the use of freshly distilled water does not obviate the necessity of observing other precautions in the preparation of solutions and their administration by way of the blood steam. Such solutions should be absolutely sterile; they should, as far as possible, be free from particulate matter (except when citrated blood is used) and the temperature at which they enter the body should be between 37 and 40 C. The optimum rate for the several solutions used appears to differ somewhat, and there is abundant clinical evidence to show that physiologic solution of sodium chloride may be introduced with greater rapidity than other solutions, perhaps as rapidly as 1,000 cc. per hour, provided the condition of the patient's heart will permit. With other solutions the maximum limit of administration should be 300 cc. per hour. The fact that it is possible to give injections at any speed without producing reactions in every case has always been a stumbling block to the intern. When he is remonstrated with for injecting 50 per cent dextrose as rapidly as he can push down the plunger of the syringe he usually responds, "But I have given thirty injections in this way without any difficulty," and his feelings are greatly hurt when the patient has a chill after the thirty-first and he is blamed for giving the solution too rapidly.

SUMMARY

Over a period of four years and three months, no chill has followed the introduction of physiologic solution of sodium chloride into the veins of patients at the New York Hospital. This solution was made with New York City tap water freshly distilled once, in a Barnstead still run by steam and operated during a large part of the period at the full capacity of the apparatus. This experience demonstrates with certainty that singly distilled water can be used with safety in the preparation of solutions for intravenous administration and that "triply distilled water" is truly a "fetish" in that it is a "material object regarded with awe, as having mysterious powers residing in it . . . and from which supernatural aid is to be expected." [15]

CONCLUSIONS

1. The use of triply distilled water in the preparation of solutions for intravenous administration is not necessary.

2. The use of freshly (and properly) distilled water in the preparation of solutions for intravenous administration is essential.

3. Solutions introduced directly into the circulation, other than physiologic solution of sodium chloride, should be administered at a rate not to exceed 5 cc. per minute.

525 East Sixty-Eighth Street.

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AN IMPROVED CONCENTRATION TEST OF RENAL FUNCTION

II. A SIMPLE METHOD FOR MEASURING PROTEINURIA

F. H. LASHMET, M.D.
AND
L. H. NEWBURGH, M.D.
ANN ARBOR, MICH.

In a previous publication [1] we pointed out that the specific gravity of the urine is an accurate measure of renal function if several standardized conditions are in effect. It was also intimated that this classic way of examining the kidneys was no longer popular because disregard of several fundamental features had destroyed the value of the readings. Among these is the failure to recognize the effect of albuminuria on the specific gravity. In the earlier paper it was shown that the specific gravity is increased 0.003 by the presence of 1 per cent of dissolved protein. It is then essential to know the extent of the albuminuria so that its effect may be subtracted from the observed specific gravity. The method employed by us in our earlier work was accurate but too laborious for use by the practitioner. We were, however, unable at that time to offer a practical substitute. The present communication describes a simple and rapid procedure for measuring the albuminuria.

Folin [2] proposed a method which depends on the turbidity, or cloud, produced by thiosalicylic acid when added to a solution containing protein. By comparing the turbidity of urine produced in this way with that of a solution of known protein content, the exact percentage of protein in the urine can be determined. Folin prepared a solution of sheep's serum containing 0.1 per cent of protein. This was the standard protein solution. The objection to this method, from the point of view of the practitioner, is the difficulty in preparing and preserving the standard solution of sheep serum protein.

TECHNIC

A similar and permanent turbidity has been secured by using only inorganic substances.

Stock Solution.—To about 200 cc. of distilled water in a 500 cc. volumetric flask, 50 cc. of 0.1 normal sodium hydroxide solution and 8 Gm. of copper sulphate (hydrous) are added. The 500 cc. volume is made up with distilled water.

Standard Solution.—After shaking the stock solution vigorously to insure a uniform suspension, exactly 2 cc. of this mixture is transferred by a pipet to a test tube (16 mm. in diameter), 23 cc. of distilled water is added. The turbidity of this mixture is identical with that produced by a 0.1 per cent solution of protein when thiosalicylic acid is used, as described by Folin. Fresh standard tubes may be prepared as desired for use from the stock solution. A permanent standard tube [3] may be prepared by drawing out the end of the test tube and sealing it in the flame. In either case the tube must be shaken and inverted several times just before using.

In order to determine the percentage of protein in urine, 1 cc. of filtered urine is placed in a test tube of the same diameter as that of the standard tube. Twenty-four cubic centimeters of thiosalicylic acid (2 per cent) is added. Comparison of this tube with the standard tube should not be made sooner than three minutes, or later than ten minutes, after the thiosalicylic acid has been added. If the turbidity of this mixture is the same as that of the standard tube, the urine contains 0.1 per cent of protein. If the turbidity is greater than that of the standard tube, the urine must be diluted and the procedure repeated until a "match" is obtained. Correction must then be made for the final dilution. For example, if the urine dilution is 1 to 10 (1 cc. of urine + 9 cc. of water) before 1 cc. of the diluted urine and 24 cc. of thiosalicylic acid matches the standard tube, then the urine contains 1 per cent of protein. In other words, the dilution is multiplied by 0.1 to obtain the percentage of protein present. After a little experience, one can estimate the dilution necessary from the turbidity obtained at the first trial. Usually only one dilution is necessary.

Since 1 per cent of protein raises the specific gravity of the urine 0.003, it is evident that any proteinuria below 0.3 per cent does not need to be considered in correcting the observed specific gravity of the urine in the concentration test. The specific gravity of most urines accordingly will not require correction for albuminuria.

From the Department of Internal Medicine, University of Michigan Medical School.

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Clinical Notes, Suggestions and New Instruments

PERIODIC EDEMA OF HAND WITH SEVEN DAY CYCLE: TREATMENT WITH SYMPATHETIC GANGLIONECTOMY

WALTER D. ABBOTT, M.D., DES MOINES, IOWA

The phenomenon of angioneurotic edema is not uncommon, but the appearance of a circumscribed edema in the same area of the body with a definite cycle warrants close investigation. Such a condition, occurring independently of the menstrual cycle and without a febrile course, relegates itself to a bizarre group of disease entities over which there is much contention regarding the proper classification.

Quincke [1] in his original description of acute circumscribed edema, mentioned the tendency to recurrence in the same spots at regular intervals. Then Matas [2] reported a periodic case of daily swelling of the upper lip, beginning at 8 a. m. and completely subsiding by 5 p. m. He also quoted Riehl's case with a fifteen day cycle. Osler [3] mentioned the regularity of attacks, occurring in seven, twelve or fourteen day cycles. Then Collins,[4] in a review of the literature, reported three cases and suggested that this disorder might be the result of an imbalance of the autonomic nervous system. At that time the chief remedies were massive doses of quinine and removal to a different climate. Kermauner,[5] Thost [6] and Goldschmidt [7] reported isolated cases with fairly well marked periodicity, and in 1914 Cohen [8] reviewed seven cases in which he stressed the imbalance of the autonomic nervous system by referring to this condition as a vasomotor or autonomic ataxia.

Cohen [8] commented on the difficulty in classifying these phenomena and suggested the term angioneural arthrosis in lieu of intermittent hydrarthrosis, periarthrosis and cyclic angioneurotic edema. A few years later, Bierring [9] collected a series of cases in which there was intermittent swelling of a joint or extremity, and, more recently, Weismann-Netter [10] reported a case of periodic hydrarthrosis of the knee which was relieved by injections of ergotamine tartrate.

From the Iowa Methodist Hospital.

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Many authorities have considered a cyclic edema to be one of the bizarre manifestations of allergy which may be the result of foreign protein or sunlight, heat, cold or focal infection and trauma.

Lewis and Grant, following their work on vascular reactions of the skin to injury,[11] concluded that various skin reactions are due to the release of diffusible substances from the skin following trauma. The skin reaction is similar to that following the introduction of histamine into the skin, and this substance was found in the tissues of the body by Barger and Dale.[12] Duke[13] stated that allergic reactions might be the result of absorption of histamine-like substances from the intestinal tract. Horton and Brown,[14] in their treatise on cold allergy, concluded that "a physical agent, such as cold, might break down certain molecules in the skin, subcutaneous tissues, or muscles, with the liberation of histamine or histamine-like bodies, which when carried into the general circulation would produce the typical histamine effects."

On the assumption that the injection of increasing doses of histamine would induce refractory periods during which reactions would not occur, the following case was treated with histamine at the Mayo Clinic in 1928, with relief for a period of six months, and was reported by Mueller[15] in 1930:

REPORT OF CASE

A Jewish woman, aged 30, unmarried, was referred to my service by Dr. Joseph Brown of Des Moines with the hope that sympathetic ganglionectomy would be of value. The woman was in perfect health except for a swelling and discoloration of the entire left hand occurring on alternate Wednesdays and lasting one week. The following week, the patient would be entirely free from symptoms. This condition had persisted for eighteen years, and twice during this interval there had been relief of symptoms for a period of two years. There was no relation to the menstrual periods, which were rather irregular. She had been given injections of foreign protein and solution of pituitary without benefit.

In 1928, the patient was given increasing doses of histamine at the Mayo Clinic with relief for a period of six months.

May 27, 1931, she was admitted to the neurosurgical service and presented a swollen, discolored hand in which the skin was very shiny. She complained of pain to a moderate degree and of limitation of joint motion in the fingers of the left hand. On Wednesday morning, the day of the onset of the cyclic edema, the surface temperature of the right hand was 34.5 C. (94 F.) and of the left hand 32 C. (89.6 F.). A procaine hydrochloride injection of the left stellate and second thoracic sympathetic ganglions was performed. Within a few minutes, the temperature was raised to 34.5 C. (94 F.) in the left hand, while the temperature of the right hand remained the same. The swelling, discoloration and limitation of joint motion disappeared, and the patient estimated a 75 per cent relief of pain. An hour after the injection, the temperature of the left hand was 35.5 C. (95.9 F.) and the patient was able to shuffle a deck of cards. In six hours the pain, swelling and discoloration returned, and the surface temperature dropped to 32.5 C. (90.5 F.). The following day, the hand returned to its previous condition.

On August 20, the injection was repeated on Friday, the third day of the cycle of edema, and within an hour the pain, swelling and discoloration disappeared with a rise in surface temperature of 3 degrees C.

A cervicothoracic sympathetic ganglionectomy was performed, September 15, which was the Tuesday preceding the onset of the cycle of swelling. The following morning the hand was normal in appearance and has remained so to the present. There has been a rise in surface temperature of the left hand from 32.5 (90.5 F.) to 36.5 C. (97.7 F.).

This case is presented to illustrate the benefit of sympathetic ganglionectomy in cases of vasomotor instability. It is obvious that all such cases should be carefully selected before a major surgical procedure is attempted.

Equitable Building.

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URTICARIA DUE TO SENNA LEAVES

LESTER HOLLANDER, M.D., PITTSBURGH

Mrs. N. J., aged 41, American, a housewife, consulted me, Aug. 5, 1932, on account of an evanescent, extremely itchy eruption which affected her lower extremities, especially her thighs. It began sometime during the month of May, 1932, and was always worse at night and about the time of waking in the morning. The patient stated that about two hours after retiring she would generally wake up on account of the intensity of the itch, and at that time fairly good sized welts would be present on her legs, and they would persist during the night and at times after she got up in the morning. Later during the day the itching would subside, only to return and repeat the cycle during the night.

General examination revealed nothing of importance, except the remnants of some scratch marks and a few indefinite wheals, sufficient, however, to make the diagnosis of urticaria. Laboratory examinations, including chemical examination of the blood, blood count, serologic studies and urine examination, were entirely negative. Questions regarding her habits of diet, of wearing apparel, of night clothes, of bed clothes, and recent changes regarding them, revealed nothing of importance.

The patient was then skin tested, and a number of positive reactions were found: milk, kidney beans, corn, English walnut, tomato, silk, wool, and house dust. A strict regimen was then instituted, all the foods mentioned and articles of wearing apparel being eliminated, but the urticaria did not disappear. The question of house dust was eliminated, as the patient went away to the seashore for a summer vacation, still adhering to the prescribed regimen, but still there was no relief from the urticaria.

On her return, at the end of September, I was considering the trial of elimination diets, when I again went over her history. The outstanding feature of this was the reassertion of the fact that about two hours after the patient retired she was usually wakened by intense itching, and the reassertion that her hives were worse then than at any other time. These awakening periods apparently had no relation to the time of her retiring, which varied from about 11 p. m. to about 2 a. m. Her habits of the evening were then established: Dinner was usually taken at about 7 o'clock, the time difference of this varying about fifteen to twenty minutes one way or another. That, of course, seemed of some importance at this time, as the patient took no food between her dinner in the evening and the following morning.

Then preparations for going to bed were discussed. These consisted of the usual bathing and toilet procedures. At this time she also mentioned the fact that just before retiring she was in the habit of taking four or five senna leaves, which she chewed and swallowed because she believed that it had a beneficial effect on her bowels.

At first I was going to disregard this, especially when I was told that she had been doing this for about fifteen years, but a recapitulation of her history, with the definiteness with which the cycle of events occurred, led me to the trial of placing the patient on a general diet with the elimination of the senna leaves at night. There was an instantaneous response to this, her urticaria disappearing.

After fourteen days of absolute freedom from the hives, the patient was asked to repeat the chewing of the senna leaves at the time of retiring, and the urticaria returned in the previously described cycle.

There are two points of interest in this report. The first deals with the question of history taking: In urticaria, in eczema, in contact dermatitis, in trade or professional dermatoses, much more can be learned by analyzing an intelligent patient's recital of events than would appear at first sight. Only after a careful consideration of a patient's uninterrupted recital

From the Pittsburgh Skin and Cancer Foundation.

should one start questioning the patient. Too often, as happened in this case, is it assumed that the statement of a patient is not reliable and that the symptoms are imagined. I missed the lead which was given by the patient in the statement that the symptoms occurred about two hours after retiring, because of the assumed reason that the normal relaxation of the body and the warmth of the bed clothes were responsible for the occurrence of the hives at that time, and also because I suspected a nervous element in this case. Later, when the skin tests showed positive reaction to wool, silk and house dust, I assumed that these played the important rôle, discounting the fact that the localization of the symptoms would be pretty much against this hypothesis.

The second point of importance deals with the following: For fifteen years this patient had taken senna leaves without having any appreciable amount of trouble. Then suddenly the gradually increasing urticaria developed. Naturally, the question arises, "Is this an example of an acquired hypersensibilization, and is it comparable to the experiments of Prof. Bruno Bloch?"

631 Jenkins Arcade Building.

MESENTERIC CYST IN A CHILD

JOHN A. NUNN, M.D., AND JOHN D. GLECKLER, M.D.
SAN ANTONIO, TEXAS

Our purpose in this paper is to report a case of mesenteric cyst, which, judging from the current literature, is a relatively infrequent condition and, from the textbooks, nonexistent; also to advance a possible explanation for the condition in a case in which the usual pathologic changes did not exist.

J. T., a boy, aged 3 years, seen, Aug. 29, 1932, had always been in good health until three months before he came to us. His family and birth histories were negative. He weighed 8½ pounds (3,855 Gm.) at birth; he walked at 9 months; he was breast fed for three months and then fed whole cow's milk formula. His parents had noticed a left sided hernia since he was 1 month old. He had had none of the contagious diseases of childhood. His parents stated that the hernia had been small and reducible until three months before we saw him, since which time it had grown very large and could not be reduced. The parents noticed that the abdomen had been increasing in size for the past three months. The abdomen had rather rapidly increased in size up to August 29, and for the two or three weeks preceding that date it had caused considerable respiratory embarrassment. He was up and about until two weeks before he came in, but during the last two weeks he had been unable to walk. For two months his bowels had been constipated and laxatives had been required. His appetite had been poor for two or three months.

The child was well nourished and well developed; he had some difficulty in breathing. Examination of the heart, lungs, eyes, ears, nose, throat and extremities showed nothing abnormal. The abdomen was very large, symmetrical and tense; the superficial veins were distended, and the costal margins were flaring. On palpation, there was no tenderness or rigidity and no masses were felt. The liver and spleen were not enlarged. On percussion, dulness extended from midway between the umbilicus and ensiform cartilage to the pubic bone, the entire width of the abdomen, and a fluctuation wave was easily elicited. The left scrotum was very large and tense, and the left testicle could not be felt.

Eight days before coming to us he was examined in a hospital in a neighboring city. The physicians there did a paracentesis of the abdomen and withdrew 2 quarts of bloody fluid, after which the child was comfortable for three or four days, but the fluid rapidly collected again. Examination of the urine was entirely negative. The intradermal tuberculin test with 0.2 mg. of Koch's old tuberculin was negative. A roentgenogram of the chest showed the lung markings normal, a heart of normal size, shape and position, and normal mediastinal shadows. A roentgenogram of the abdomen, flat plate only, showed the entire abdomen as a homogeneous shadow with the exception of a column of gas extending up the right side to the diaphragm and across the midline to the usual position of the splenic flexure of the colon. At operation we found that this was the location of the descending and transverse colons. The blood Wassermann reaction was negative. A blood count showed: hemoglobin, 70 per cent; red blood cells, 4,830,000; white blood cells, 14,250; total neutrophils, 57 per cent; lymphocytes, 31 per cent; eosinophils, 1.5 per cent; basophils, 0.5 per cent; monocytes, 9.5 per cent.

Conditions to be considered in this case were: First, tuberculous peritonitis, because that is the most frequent cause of ascites in children who have no advanced cardiac or renal disease. The intradermal tuberculin test with 0.2 mg. of old tuberculin was negative, which would make such a diagnosis doubtful. Second, some obstruction to the portal circulation such as may be caused by peritoneal adhesions, enlarged lymphatic glands or a benign or malignant tumor, which might also involve the lymphatic glands. Third, some intra-abdominal or retroperitoneal cyst having its origin from the kidney, spleen or misplaced embryonal tissue. However, we felt that the case was one of ascites.

September 2, we did a paracentesis of the abdomen and withdrew a quart of bloody fluid, which coagulated on standing. Microscopic examination of this fluid showed many red blood cells and nothing else. Since the fluid had collected so rapidly, following the paracentesis eight days before, and was causing so much respiratory distress, we decided that an exploratory operation was imperative.

Operation showed a cystic mass displacing all peritoneal structures, including the descending and sigmoid colons, to the right side of the abdomen. The cyst was punctured and emptied gradually. The fluid was similar to that withdrawn by paracentesis. The posterior wall of the cyst was formed by all retroperitoneal structures to the left of the vertebral column from the diaphragm to the brim of the pelvis; its anterior wall, by the peritoneum and colon. On the posterior wall of the descending colon a handful of necrotic material resembling an organized blood clot was found very loosely adherent to the wall. This was easily removed. The peritoneal opening was closed and a drain placed in the left flank retroperitoneally. It was decided to repair the hernia at the same time, and when this was done a portion of the sigmoid colon was found in the hernial sac. This was reduced. Since the left testicle appeared rudimentary, the entire contents of the left scrotum were removed and the defect in the anterior abdominal wall was closed.

A pathologic report by Dr. B. F. Stout was as follows: The testicle was rudimentary; the portion of the cyst wall removed at operation had no special features and consisted mostly of a relatively thin fibrous tissue. The necrotic mass removed showed small islands of cells which suggested either lymphoid or possibly small cell sarcoma. The tissue took the stain very poorly, owing to necrosis, so that the structure of the cell could not be studied sufficiently to establish its identity. The remainder of it was mostly necrotic blood clot and fibrous tissue. The fluid from the cyst showed the enzyme amylase, but the presence of this could be explained by the presence of blood.

As a possible source of the cyst we have considered traction of the hernia on the retroperitoneal attachments of the descending colon, which might have caused a tearing of this attachment with consequent exudate and the establishment of a circle of empty space filling with tissue exudate, which would cause pressure irritation and thus more exudate. This is a possible explanation and, as no further cause could be found, may have to be accepted as the only one. It is unusual for the descending colon to fill a hernial sac, but it is not difficult, once it is in the sac and filled with feces, for it to cause traction on the upper portion.

The wound in the retroperitoneal space continued to drain the blood-stained fluid and after about ten days a purulent fluid. Three weeks after operation the child was allowed to return to his home in a distant town under the care of the family physician, who reported, ten weeks after the operation, that the wound had entirely healed, the abdomen had maintained its normal contour, and no masses could be palpated. The child was up and about, apparently in the best of health. We feel that the infection in the retroperitoneal space destroyed the secreting surface of the cyst wall and that the repair of the hernia, eliminating the traction on the upper portion of the colon, effected a cure of his condition. Five months later the child was reported still in good health.

Medical Arts Building.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

ESTROGENIC SUBSTANCES: THEELIN

The introduction into therapeutics of commercial preparations with active estrogenic properties marked what appeared to be a new phase in the treatment of female sexual disorders. These new preparations, unlike those with which the market had been replete for many years, produced striking and concordant effects when injected into animals. It was anticipated that these products might be of great value in the therapy of menstrual and related disturbances; their clinical use spread widely and rapidly, and observations accumulated in profusion. But the early enthusiasm began to wane as it became evident that the therapeutic usefulness of the estrogenic preparations had been greatly overestimated; the effects of injections in human beings were in the great majority of cases neither striking nor concordant; and in those cases, too few, unfortunately, in which an effort was made to control the observations carefully, the results appeared to be even less notable. Despite their extensive employment, the indications for the clinical use of Theelin and related products are at the present time only imperfectly understood. With a view to establishing, if possible, the indications for and limitations of endocrine therapy of this type, the following review was prepared, and adopted by the Council for publication:

In 1929, Doisy, Veler and Thayer [1] announced the isolation from the urine of pregnant women of a crystalline preparation capable of inducing estrus in the ovariectomized sexually mature rat. The preparation was found both by chemical and by physiologic tests to be indistinguishable from highly potent extracts of the ovarian follicular fluid, except in regard to crystalline form and higher activity. As it appeared likely at that time that the crystalline preparation might have a wide field of clinical usefulness, Dr. Doisy in cooperation with Dean Schwitalla [2] of St. Louis University endeavored to introduce the product in a manner that would prevent its unscientific exploitation. The Council recognized the right of Doisy to name his crystalline product and voted to recognize the name "Theelin" proposed by him "as the nonproprietary N. N. R. name for the crystalline ovarian hormone made by the process of Doisy." Later, in order to avoid confusion, the Council voted to modify the previous definition and to recognize "Theelin" as the "nonproprietary name for the crystalline (dioxy) ovarian hormone as described under this name by Doisy," and "Theelol" [3] as the "nonproprietary designation for the crystalline (trioxy) ovarian hormone as described under this name by Doisy. . . ."

Parke, Davis and Company was licensed by the St. Louis University to manufacture Theelin; the firm presented the product for consideration by the Council. Theelin, Parke, Davis & Co., was claimed to be "an aqueous solution of crystalline ovarian follicular hormone adjusted to contain 50 rat units in each cubic centimeter." The preparation was said to be standardized by the three-injection method of Allen and Doisy; [4] the rat unit was defined as the minimum amount necessary to induce estrus with complete cornification of the vaginal mucosa as judged from a smear, in 75 per cent of a large group of ovariectomized sexually mature rats (150 ± 20 gram body weight). Three injections were made at intervals of four hours. The therapeutic indications were stated to be amenorrhea, oligomenorrhea, hypomenorrhea, natural and artificial menopause, and retarded development of secondary sex characters. The indicated dosage was from 50 to 100 rat units a day for varying periods up to several weeks. No satisfactory evidence of clinical usefulness was submitted at that time by the manufacturer. Subsequent evidence submitted was considered not acceptable by the Council.

It is the purpose of the present report briefly to review the literature available to the Council on the female sex "hormones" in general. This survey is of course not exhaustive; but the Council believes that consideration of Theelin alone as a therapeutic agent cannot be satisfactory without an appreciation of the present status of our knowledge on the interaction of the various endocrine factors concerned with sexual physiology in the female.

When Theelin was introduced, it was thought to constitute, if not the only, then the chief,[5] ovarian factor in the regulation of the sexual cycle. It is perhaps unfortunate that the remarkable effects induced in animals led to its introduction for therapeutic use in the human being without adequate preliminary trial. For the most part this has resulted in a profusion of uncontrolled observations and has led to great confusion; considerable difficulty was encountered in evaluating the results. The possibility that a preparation as active as Theelin is in animals might do considerable harm in its unconsidered clinical use has apparently not received the attention it deserves. Reports have recently appeared in the literature indicating that in experimental animals possibly serious damage may result from the prolonged administration of estrogenic substance; these will be discussed below.

The evidence accumulated so far points to the existence of as many as five, and possibly more, special endocrine factors involved in the female sexual cycle. All these appear to be essential to its normal operation, apparently in varying proportions at different periods of the cycle. It is important to note here that, in the occurrence of these factors and in the incidence or predominance of their effects, species differences play a very significant part; in general this is noted in the text, but space does not permit uniform emphasis throughout.

ANTERIOR PITUITARY GLAND

That the anterior hypophysis is in some way related to the sexual cycle was long suspected; this dates from the observations of Fröhlich [6] (1901), who first described the syndrome, since known by his name, involving aberration of bodily structure and sexual function associated with morphologic change in the pituitary. In 1909, Erdheim and Stumme [7] reported marked hypertrophy of the anterior pituitary in pregnancy. Cushing [8] and his co-workers presented further evidence of the interrelationship of the anterior pituitary and sexual function. H. M. Evans,[9] in 1924, reported that injection of extracts of the anterior hypophysis in rats resulted in disappearance of the estrual cycle so long as the extracts continued to be administered. Associated with this phenomenon, graafian follicles in the ovaries were found to have undergone luteinization. P. E. Smith and Smith and Engle [10] demonstrated the effects of hypophysectomy, of homopituitary and heteropituitary transplants, anterior pituitary feeding and the injection of anterior pituitary extracts. Zondek and Aschheim,[11] in 1927, demonstrated that, of a large series of different tissues tested, the pituitary alone appeared to be involved in these effects on the sexual organs, described below. Continuation of these studies by both groups of investigators demonstrated the dependence of normal ovarian function on the activity of the

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2. Schwitalla, A. M.: J. A. M. A. **94:** 1523 (May 10) 1930; Bull. St. Louis Univ. **27,** July, 1931; Theelin—and the Technic of Introduction of New Drugs, editorial, J. A. M. A. **97:** 1541 (Nov. 21) 1931.

3. Doisy, E. A.; Thayer, S. A.; Levin, L., and Curtis, J. M.: Proc. Soc. Exper. Biol. & Med. **28:** 88 (Oct.) 1930. Doisy and Thayer: J. Biol. Chem. **91:** 641 (May) 1931. Thayer, Levin and Doisy, ibid., p. 655; Theelin and Theelol, editorial, J. A. M. A. **97:** 31 (July 4) 1931.

4. Allen, Edgar, and Doisy, E. A.: J. A. M. A. **81:** 819 (Sept. 8) 1923.

5. Allen, Edgar: J. A. M. A. **97:** 1189 (Oct. 24) 1931.

6. Fröhlich, A.: Wien. klin. Rundschau **15:** 1901 (cited from Parkes, A. S.: Internal Secretion of the Ovary, London, 1929).

7. Erdheim, J., and Stumme, E.: Beitr. z. path. Anat. u. z. allg. Path. **46:** 1, 1909.

8. Cushing, Harvey: The Pituitary Body and Its Disorders, Philadelphia, 1912.

9. Evans, H. M.: Harvey Lectures **19:** 212, 1923-1924.

10. Smith, P. E.: Anat. Rec. **32:** 221, 1926; Proc. Soc. Exper. Biol. & Med. **24:** 131 (Nov.) 1926; 337 (Jan.) 1927; Am. J. Physiol. **80:** 114 (March) 1927; **81:** 20 (June) 1927. Smith, P. E., and Engle, E. T.: Proc. Soc. Exper. Biol. & Med. **24:** 561 (March) 1927; Anat. Rec. **35:** 22 (March) 1927; Am. J. Anat. **40:** 159 (Nov.) 1927.

11. Zondek, Bernhard: Klin. Wchnschr. **6:** 135 (Jan. 15) 1927; Med. Klin. **23:** 463 (March 31) 1927. Zondek, Bernhard, and Aschheim, Selmar: Klin. Wchnschr. **6:** 248 (Feb. 5) 1927; Arch. f. Gynäk. **130:** 1, 1927; Klin. Wchnschr. **6:** 1322 (July 9) 1927.

pituitary. Zondek proposed that the hypophysis be considered the "motor" of the ovary. While the posterior hypophysis may be involved in parturition, it is apparently not concerned with the anterior lobe effects. With the additional information furnished more recently by others, the following briefly may be considered the present status of the investigative work on the anterior pituitary factors:

The number of separate hormones produced by the anterior hypophysis cannot at present be ascertained; but the existence of several appears to be fairly well established, and a number of others have been claimed: (1) a growth factor, which is concerned with bodily growth and antagonistic in a certain degree to the sex factor(s), inhibiting the activity of the latter during the period of active growth; (2) a follicle stimulating factor, which induces growth and maturation of ovarian follicles with production of the estrus-inducing factor; (3) a luteinizing factor, which is capable of inducing extensive luteinization of ovarian follicles (when in excess, even before ovulation); (4) a factor which (in conjunction with the estrus-inducing factor) can induce uterine bleeding in monkeys (recent work casts some doubt on the existence of this principle);[12] (5) a factor which can induce mammary proliferation and lactation in rabbits.[13]

Not all investigators are agreed as to the duality of 2 and 3. Some of the more recently accumulated evidence seems to indicate the existence of two separate factors,[14] but species differences appear to play a large part in the relative predominance of the two effects.[15] It is too early at this time to attempt an evaluation of these claims and of others for still other "hormones"; of these, the existence of the growth factor and the fraction(s) having to do with follicular growth and luteinization may be considered as established. Aschheim and Zondek[16] have made extracts of the urine of pregnant women, these extracts having the combined physiologic properties of the follicle-stimulating and luteinizing factors. These they term "Prolan"; they have also prepared fractions said to have the separate properties individually and call these "Prolan A" (follicle stimulating) and "Prolan B" (luteinizing). The latter they considered identical with similar preparations made from the anterior hypophysis but this appears to be dubious,[17] particularly in view of the observation of Reichert and Evans and their co-workers[18] that substitution therapy with urinary prolan failed after hypophysectomy. Wiesner[19] has prepared extracts having similar effects which he calls Rho I and Rho II, respectively. Collip[20] has isolated from the placenta two fractions, one of which, "Emmenin," has physiologic actions similar in part to those of Prolan A, and the other of which is similar in this respect to Prolan B. Where these substances are elaborated cannot at present be decided.

Aschheim and Zondek[21] have utilized the presence of the Prolan fraction in the urine as a test for pregnancy as determined by the effect on the ovaries of immature mice. Other pregnancy tests[22] have been suggested. These methods have also been used in testing for the presence of the Prolan fraction in the blood and in the urine in the normal state and in various pathologic conditions and in estimating the amounts of estrus-inducing factor in these fluids.[23] Some of the results of these investigations are presented below.

In summary, the following actions have been ascribed to secretions of the anterior hypophysis: (1) Induction of ovulation;[24] (2) Stimulation of ovary to secretion of estrogenic substance; (3) Production of luteinization in follicles either with or without ovulation (luteinization may also be induced by direct intrafollicular injection of urine of pregnancy),[25] leading to secretion of "Progestin";[26] the anterior hypophysis is essential to the maintenance of the corpus during pregnancy;[27] (4) Induction of uterine bleeding with combined action of estrogenic substance (even without the presence of the endometrial hyperplasia characteristic of menstruation); (5) Production of mammary proliferation and lactation without the intermediation of ovarian factors;[28] (6) Production of marked hypertrophy of seminal vesicles and prostate.[29]

It is by this time well authenticated that (regardless of how many factors are involved) in the absence of a functional anterior pituitary, normal cyclic ovarian function ceases.[30]

Considerable evidence has accumulated that the hypophysis is involved in the control of metabolism. While these data appear to be far-reaching in their implications, it is too early to speculate as to their ultimate significance. This phase of the problem lies beyond the scope of this report and the extensive bibliography will not be presented or discussed here. Of interest in this connection, by way of illustration, is the recent work indicating a relationship with thyroid activity and an association with dextrose and fat metabolism. Houssay and Biasotti (Endocrinology **15**: 511 [Nov.-Dec.] 1931), for instance, have reported that hypophysectomy prevents or diminishes the glycosuria produced by pancreatectomy; implantation of anterior pituitary in such animals may then result in a rise in blood sugar. Animals which have been both pancreatectomized and hypophysectomized have lived for months with blood sugar either normal or only moderately elevated. Anselmino and Hoffmann (Klin. Wchnschr. **10**: 2380, 2383 [Dec. 26] 1931) have prepared extracts of the anterior lobe of the hypophysis which on injection cause a rise in the level of acetone bodies in the blood. The latter findings may be of especial significance with respect to the known relationship of dextrose utilization with fat metabolism.

OVARY

Preparations capable of inducing changes in the tubular tract were made from the ovary as early as 1906 by Marshall and Joly; later, Adler, Iscovesco, Fellner, Okinschitz, Seitz, Wintz and Fingerhut, Herrmann and Fraenkel, Frank[31] and others made potent preparations of whole ovary, placenta, corpus luteum or follicular fluid. Since the culmination of this work by the isolation of a crystalline estrogenic substance by Doisy, Veler and Thayer[1] (and independently by Butenandt)[32] from the urine of pregnant women, it is established that estrogenic agents can be obtained from the following sources (it is understood that the alleged identity of these agents rests only on similarity of physiologic action and in some instances on similar chemical characteristics but in no case, to the Council's knowledge, has actual chemical identity been established): (1) follicular fluid;[33] (2) corpus luteum;[34] (3) ovarian stroma (?); (4) blood of nonpregnant women at certain stages in the menstrual cycle; (5) urine of nonpregnant women; (6) blood of pregnant women; (7) urine of pregnant women (the mater-

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15. Engle, E. T.: Sex and Internal Secretions, edited by Edgar Allen, Baltimore, Williams and Wilkins Company, 1932, chapter 16; Proc. Soc. Exper. Biol. & Med. **29**: 1224 (June) 1932.

16. Aschheim, Selmar, and Zondek, Bernhard: Klin. Wchnschr. **7**: 1404 (July 22) 1928.

17. Engle, E. T.: J. A. M. A. **93**: 276 (July 27) 1929.

18. Reichert, F. L.; Pencharz, R. I.; Simpson, M. E.; Meyer, K., and Evans, H. M.: Proc. Soc. Exper. Biol. & Med. **28**: 843 (May) 1931. Evans, H. M.; Meyer, K., and Simpson, M. E.: Am. J. Physiol. **100**: 141, 1932.

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20. Collip, J. B.: Canad. M. A. J. **22**: 215 (Feb.), 761 (June); **23**: 631 (Nov.) 1930.

21. Aschheim, Selmar, and Zondek, Bernhard: Klin. Wchnschr. **7**: 8 (Jan. 1) 1928. Aschheim, Selmar: Am. J. Obst. & Gynec. **19**: 335 (March) 1930.

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23. (*a*) Frank, R. T.; Frank, M. L.; Gustavson, R. G., and Weyerts, W. W.: J. A. M. A. **85**: 510 (Aug. 15) 1925. (*b*) Frank, R. T., and Goldberger, M. A.: ibid. **87**: 719 (Sept. 4) 1926; **90**: 106 (Jan. 14) 1928; **94**: 1197 (April 19) 1930. (*c*) Frank, R. T.; Goldberger, M. A., and Spielman, F.: Proc. Soc. Exper. Biol. & Med. **28**: 999, 1931. (*d*) Frank, R. T.: J. A. M. A. **97**: 1855 (Dec. 19) 1931. (*e*) Fluhmann, C. F.: J. A. M. A. **92**: 1744 (May 28) 1929; **93**: 672 (Aug. 31), 1136 (Oct. 12) 1929; Am. J. Obst. & Gynec. **20**: 1 (July) 1930; Endocrinology **15**: 177 (May-June) 1931; Proc. Soc. Exper. Biol. & Med. **29**: 1193 (June) 1932. (*f*) Kurzrok, R.: Endocrinology **16**: 361 (July-Aug.) 1932. (*g*) Eberson, F., and Silverberg, M. H.: J. A. M. A. **96**: 2176 (June 27) 1931. (*h*) Mazer, C., and Goldstein, L.: Clinical Endocrinology of the Female, Philadelphia, 1932. (*i*) Soule, S. D.: Am. J. Obst. & Gynec. **23**: 708 (May) 1932.

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28. Corner; Riddle, Bates and Dykshorn.[13]

29. (*a*) Zondek, Bernhard: Zentralbl. f. Gynäk. **53**: 834 (April 6) 1929 (from abst. J. A. M. A. **93**: 247 [July 20] 1929). (*b*).[20]

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31. Cited from Parkes, A. S.: Internal Secretion of the Ovary, London, 1929. Frank, R. T.: Colorado Med. **21**: 123 (May) 1924.

32. Butenandt, A.: Deutsche med. Wchnschr. **55**: 2171 (Dec. 27) 1929.

33. Frank, R. T.: J. A. M. A. **78**: 181 (Jan. 21) 1922. Allen, Edgar, and Doisy, E. A.: **81**: 819 (Sept. 8) 1923. Frank, R. T., and Gustavson, R. G.: J. A. M. A. **84**: 1715 (June 6) 1925. Allen, Edgar; Pratt, J. P., and Doisy, E. A.: J. A. M. A. **85**: 399 (Aug. 8) 1925. Allen, Edgar; Pratt, J. P.; Newell, Q. U., and Bland, L. J.: Am. J. Physiol. **92**: 127 (Feb.) 1930.

34. Frank, R. T.: J. A. M. A. **81**: 1134 (Sept. 29) 1923.

nal ovaries are apparently not necessary to the production of estrogenic substance during pregnancy);[35] (8) placenta, fetal membranes and amniotic fluid; (9) male blood;[36] (10) male urine;[37] (11) certain plants;[38] (12) other materials of organic origin such as petroleum and lignite.[39] Recently, Cook, Dodds and Hewett have reported that a synthetic compound (1-keto-1:2:3:4-tetrahydrophenanthrene) has estrogenic properties; three other cyclic compounds, of which two were hydrocarbons, were found also to have this activity in addition to being definitely carcinogenic.[40]

From the observations of Frank and of others, it is apparent that the occurrence of estrogenic factor in the blood and in the urine follows certain definite curves in the normal woman; these differ during pregnancy from those found in the normal non-pregnant woman and the two former from the curves found in patients suffering from certain menstrual disorders. Certain relationships[81] have been established between the occurrence of the estrogenic and the anterior pituitary fraction (Prolan) in the blood and urine. The variations occurring in disease have to some extent also been elucidated. These studies are of the utmost importance as a basis for attempted substitution therapy, which latter, by neglect of these factors, has so far been decidedly inadequate.

These observations have served greatly to emphasize the cyclic variations that occur in the proportions of the various "hormones" in the body fluids and tissues at various times. It is evident that substitution therapy, which attempts to reproduce the natural concentration curves in the body fluids, will at no two successive times involve identical doses of a given preparation (excluding for the moment all consideration of absorption, distribution, fixation, inactivation and excretion, factors only imperfectly understood at this time). This concerns, of course, not only Theelin but all preparations purporting to contain any of the female sex "hormones." So far as the present evidence goes, such attempts at therapy as have been used in the past must usually have resulted, merely by the operation of the theory of probability, in further disruption, rather than otherwise, of an already pathologic state.

The following is a summary of the claimed actions of estrogenic substance:

1. Produces the phenomenon of estrus, consisting in hyperplasia of the vaginal wall, enlargement and hyperemia of the uterine musculature, endometrial hyperplasia, etc., on injection (or ingestion of much larger quantities) into sexually mature animals, normal or castrate.

2. Causes premature opening of the vagina and general hypertrophy of the tubular tract, with ensuing estrus, when administered to immature rats and mice (similar effects are general in other species).[40a]

3. Induces uterine bleeding, simulating menstruation, in immature and mature rhesus monkeys, in the presence of an active anterior hypophysis or on the injection of active extracts thereof.[41]

4. Produces moderate mammary hypertrophy on repeated injection, but usually does not lead to lactation. (Kunde et al. report one case of lactation in a bitch following injection of estrogenic substance.)[42]

5. If long continued at high dosage may inhibit ovulation.

6. Prevents normal growth of the anterior hypophysis and of the ovaries and results in fibrotic alterations of the ovaries, thyroid hyperplasia and other changes on prolonged administration to immature animals (in young rats bodily growth rate is diminished, testes or ovaries are markedly smaller than normal,[43] but daily administration of Theelin or Theelol to adult rats for twenty-five days does not sterilize them).[44]

7. Can prevent conception in guinea-pigs[45] and in rats, and in large doses may interrupt early (but not late) pregnancy in these animals.[46] (This apparently does not hold for all species.)

8. Enhances the rhythmic contractility of the uterus.[47]

9. Sensitizes the uterus to the action of the posterior pituitary oxytocic hormone.[48] (Jeffcoate[35] claims that Theelin, Parke, Davis & Co., does not have this effect on the isolated organ.) (The posterior hypophysis is not necessary to parturition in the cat or in the rat.)[49]

10. Produces changes in the endometrium in small doses, necessary to the subsequent action of corpus luteum, but in large doses inhibits the action of corpus luteum in causing progestational proliferation of the endometrium.[50]

11. Increases the oxygen consumption of the immature mouse uterus but not of the mature organ.[51]

12. Diminishes the coagulation time in hemophilia.[52]

13. May neutralize tetanus toxin in vitro (?).[53]

14. Long continued administration to mice, of a strain in which normally the females only develop spontaneous mammary adenocarcinomas, appears to predispose to development of such malignant tumors in the males.[53a]

CORPUS LUTEUM

As stated before, an estrogenic fraction has been obtained from this source. More recently, Allen and Corner[54] have prepared from the corpus luteum highly potent but unstable extracts, devoid of estrogenic activity, and having very interesting physiologic properties. They call this preparation "Progestin." Independently, Hisaw and his co-workers[55] have also prepared a potent product of a similar nature ("Corporin").[56]

The following effects have been ascribed to "Progestin":[57]

1. That it enhances the endometrial hyperplasia prepared by the estrogenic substance and sensitizes the uterine mucosa to nidation by the ovum.[58a]

2. That it induces mucous transformation of the superficial layers of the vaginal mucosa characteristic of pregnancy (this effect has also been ascribed to estrogenic substance).[58b,c]

3. That it inhibits the normal rhythmic contractility of the uterus.[47]

4. That it inhibits the effect of estrogenic substance, of posterior pituitary extract, and of combinations of the two on uterine contractility.

5. That it inhibits the "Prolan A" effect on the ovary, preventing ovulation.

6. That it can prolong gestation beyond the normal for a given species.

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37. Laqueur, E.; Digemanse, E.; Hart, P. C., and de Jongh, S. E.: Klin. Wchnschr. **6:** 1859, 1927.
38. Mazer, C., and Goldstein, L.: Clinical Endocrinology of the Female, Philadelphia, 1932.
39. Doisy, E. A.: Sex and Internal Secretions," Baltimore, 1932, chapter 10.
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40a. Allen, Edgar, and Doisy, E. A.: Am. J. Physiol. **69:** 577 (Aug.) 1924.
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48. Bourne and Burn: Lancet **2:** 1020, 1928.
49. Allen and Wiles, cited from Marshall, F. H. A.: Brit. M. J. **2:** 232 (Aug. 6) 1932. Smith, P. E.: Am. J. Physiol. **99:** 345 (Jan.) 1932.
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52. Birch, Carroll LeFleur: Proc. Soc. Exper. Biol. & Med. **28:** 752 (April) 1931; J. A. M. A. **97:** 244 (July 25) 1931; **99:** 1566 (Nov. 5) 1932.
53. Immamura: Acta Med., Kaijo **12:** 249, 1929 (cited from Follicular Antitoxin and the "Reynals Factor," Current Comment, J. A. M. A. **98:** 323 (Jan. 23) 1932).
53a. Lacassagne, M. A.: Compt. rend. Acad. d. sc. **195:** 630 (Oct. 10) 1932.
54. Allen, W. M., and Corner, G. W.: Proc. Soc. Exper. Biol. & Med. **27:** 403 (Feb.) 1930. Allen, W. M.: Am. J. Physiol. **92:** 174 (Feb.) 1930.
55. (*a*) Hisaw, F. L.: J. Exper. Zool. **42:** 411 (Oct.) 1925; Proc. Soc. Exper. Biol. & Med. **23:** 661 (May) 1926. (*b*) Hisaw, F. L.; Meyer, R. K., and Fevold, H. L.: Proc. Soc. Exper. Biol. & Med. **27:** 606 (March) 1930 (cited from Allen).[5]
56. Hisaw, F. L.: Sex and Internal Secretions, Baltimore, 1932, chapter 11.
57. Smith, G. V. S., and Smith, O. W.: J. A. M. A. **97:** 1857 (Dec. 19) 1931.
58. (*a*) Hisaw, F. L.; Meyer, R. K., and Fevold, H. L.: Proc. Soc. Exper. Biol. & Med. **27:** 400 (Feb.) 1930. (*b*) Meyer, R. K., and Allen, W. M.: Science **75:** 111 (Jan. 22) 1932. (*c*) Harris, R. G.: ibid. **76:** 408 (Nov. 4) 1932.

7. Smith and Smith claim that it increases the urinary output of estrogenic substance but Frank was unable to confirm this.

8. That it inhibits uterine bleeding in rhesus monkeys and apparently also in man.[59]

9. That it antagonizes the estrus-inducing effect of Theelin, etc. (This has also been noted on feeding whole corpus luteum.) [60]

Evidence that more than one factor may be involved in the foregoing effects also exists, but this is inconclusive. Hisaw [56] has prepared a fraction ("Relaxin") which, during estrus or in conjunction with estrogenic substance, causes resorption of the symphysis pubis in the pocket gopher and relaxation of the pelvic ligaments in the guinea-pig. Neither the principle nor the effect has been demonstrated in man. (The effect has been said to be due to estrogenic substance alone.)

Anterior pituitary extracts can produce any of the effects described by follicular stimulation or by luteinization of the ovary, resulting in secretion of the estrogenic and corpus luteum factors.

ABSORPTION, DISTRIBUTION AND EXCRETION OF ESTROGENIC SUBSTANCE

This phase of the problem, despite its great importance and the wide clinical use of Theelin and similar preparations, is imperfectly understood. Comparatively little attention has been paid to the subject, and the data at hand are conflicting and confusing.

Ziserman [62] have noted that, after injection of a single large dose into a patient, large amounts could be recovered from the urine shortly thereafter, but that when the same dose was distributed in fractions over twenty-four hours, only traces could be detected in the urine.

Fee, Marrian and Parkes [63] investigated this problem in the heart-lung-kidney preparation. They added 100 or 200 mouse units to the circulating blood and assayed the blood and urine. Only about 1 per cent of the injected dose was found in the urine; the substance disappeared from circulating blood rapidly. Incubation of standing blood at 37 or at 20 C. did not inactivate added estrogenic substance in three hours, although it was completely inactivated in a much shorter time in the circulating blood. Only traces were found in the heart and lung tissues. These workers suggest the possibility of oxidative destruction in the lungs. In view of the stability of Theelin to oxidation, it seems probable that the explanation of these results lies elsewhere; the possibility of inactivation or destruction by or in the tissues has not been sufficiently considered.

In human pregnancy, Frank found 50 mouse units of estrogenic substance per liter of venous blood as compared to 25 mouse units per liter in nonpregnant women; at the same time, the urine of pregnant women contained 10,000 mouse units per liter, whereas the urine of nonpregnant women contained only from 30 to 100 mouse units per liter. In view of the finding of tremendous quantities of anterior pituitary hormone in the blood of pregnant women (3,000 mouse units per liter), as well as

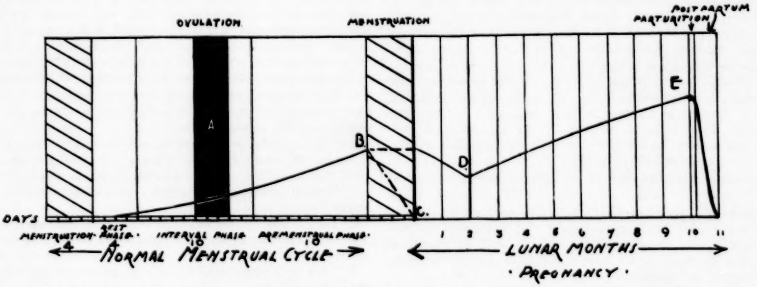

Fig. 1.—Variations in the blood content of estrogenic substance in the normal menstrual cycle and in pregnancy. *A*, estrogenic activity occasionally demonstrable at this time in 40 cc. of blood. *B*, estrogenic factor demonstrable in 94 per cent of normal women at this period in 40 cc. of blood. *C*, extent of estrogenic substance falls during menstruation. *D*, content of estrogenic principle drops in first two months of pregnancy owing to excessive excretion. *E*, estrogenic substance demonstrable by injections of whole blood into animals (reproduced through the courtesy of C. Mazer and L. Goldstein [23b]).

Frank has found in normal women that 1 mouse unit of estrogenic substance can be obtained from 40 cc. of blood, between seven days before menstruation and the onset of menstruation. No test can be obtained from this quantity of blood at other times. A total of from 800 to 1,500 mouse units may be obtained from the urine throughout the cycle, with maxima at the presumable time of ovulation (about twelve to fourteen days from the onset of the preceding flow), and from one to two days before the onset of the succeeding menstruation. The injection of 5,000 mouse units subcutaneously had no demonstrable effect on the amount recoverable from the urine of a normal woman. After the intravenous injection of 2,000 mouse units into rabbits, only 1 mouse unit in each 4 cc. of serum could be found after one hour and none at all thereafter. After subcutaneous injection of 2,000 mouse units,[61] 1 mouse unit was found in 5 cc. serum at the first hour and none thereafter. After 3,000 mouse units by vein to a rabbit, 1 mouse unit was found in 40 cc. blood after twenty-four hours; extracts of all the organs were inactive except for a total of 2 mouse units in the liver.

Allen found that after subcutaneous injection of 1,500 mouse units into each of two monkeys, one fifth of the injected dose could be recovered from the urine in two days. Mazer and

more estrogenic factor, it appears probable that increased production accounts for the larger quantities present. The placenta may be viewed with suspicion in this regard. Recent evidence indicates that the ovaries are not necessary to the production of estrogenic substance during pregnancy,[35] but the follicles are apparently the chief source in the nonpregnant animal.[64] G. Van S. and O. W. Smith, as already noted, found that "Progestin" increases the urinary excretion of injected estrogenic substance in rabbits; but the rôle of the corpus luteum in this respect has not been fully elucidated.

MENSTRUATION

Since it is for disorders of menstruation more than for any other condition that the preparations that have been discussed are chiefly used clinically, it is thought that a brief review of the more recent concepts in this field will be germane to the discussion which follows.

The difficulties involved in studying menstruation lie largely in the fact that the phenomenon is restricted to primates and can be studied, man excluded, only in monkeys and apes. Although forms of uterine bleeding, involved apparently in furnishing nutrition to the ovum, are of quite general occurrence and have an ancient phylogeny, as Hartman [65] has pointed out,

59. Smith, P. E., and Engle, E. T.: Proc. Soc. Exper. Biol. & Med. **29:** 1225 (June) 1932. Smith and Smith.[57]
60. Macht, D. D., and Stickels, A. E.: Proc. Soc. Exper. Biol. & Med. **27:** 427 (Feb.) 1930; **28:** 801 (May) 1931.
61. Frank, R. T.; Goldberger, M. A., and Spielman, F.: Proc. Soc. Exper. Biol. & Med. **29:** 1229 (June) 1932.
62. Mazer, C., and Ziserman, A. J.: M. J. & Rec. **135:** 35 (Jan. 6) 1932.
63. Fee, A. R.; Marrian, G. F., and Parkes, A. S.: J. Physiol. **67:** 377 (July 25) 1929.
64. Marshall, F. H. A., and Wood, W. A.: J. Physiol. **58:** 74 (Oct.) 1923.
65. Hartman, C. G.: J. A. M. A. **97:** 1863 (Dec. 19) 1931.

the relationship of the latter phenomenon to the process occurring in the human being has not yet been adequately elucidated.

Recently, Corner, Allen and Hartman and their respective co-workers have studied menstruation in the rhesus monkey. Corner [66] has pointed out that menstruation in the monkey frequently occurs without ovulation and is therefore dependent neither on the corpus luteum nor on the premenstrual changes in the endometrium, which are in part at least induced by the corpus luteum. Ovulation in the monkey when it does occur takes place twelve or fourteen days before the onset of the succeeding menstruation. Edgar Allen [41] reported uterine bleeding in castrated monkeys following cessation of injections of estrogenic substance. Hartman, Firor and Geiling [12] reported that the uterine bleeding induced in both normal and castrated monkeys by the injection of estrogenic substance was completely abolished by hypophysectomy. The injection of anterior lobe extracts which had neither the follicle-stimulating nor the luteinizing effect, or the implantation of anterior hypophysis restored the action of estrogenic substance. The threshold for bleeding is far below the dose necessary to produce the changes characteristic of estrus. These authors point out that bleeding may result from a uterus that shows no visible microscopic change in the mucosa. Hence the endometrial proliferation normally characteristic of the premenstrual period is not necessary to bleeding. If this is true also in the human being, it must be decided what benefit for the patient is to be attained from the induction by therapeusis of bleeding alone. Hartman and his co-workers believe that a special principle of the anterior pituitary is involved in conjunction with the action of the estrogenic principle in producing the bleeding, but Saiki's results cast some doubt on this hypothesis.

It is well known that the surgical removal of the corpus luteum in the human being results in the onset of menstruation from twelve to thirty-six hours thereafter. In extension of this observation, Corner has found that "Progestin" inhibits menstruation.

These observations cast doubt on the long accepted thesis that bleeding is of fundamental importance in the human sexual cycle and emphasize the desirability of greater caution in the treatment of disorders of menstruation. Some sign or signs in addition to bleeding may well be necessary as an indication of the existence of the normal state. These observations indicate the necessity for even greater caution than has been used in the past in evaluating the results of endocrine therapy in menstrual disorders.

Frank, Fluhmann, Mazer, Kurzrok and others have studied the cyclic occurrence of estrogenic substance and of "Prolan" in the blood and urine of normal nonpregnant and pregnant women, and of those suffering from certain menstrual disorders. A discussion of these factors is given under the clinical use of these preparations.

ASSAY OF ESTROGENIC PREPARATIONS

Allen and Doisy,[67] in their work on the isolation and purification of the estrogenic principle from liquor folliculi, utilized as a method of assay the phenomenon recorded by Stockard and Papanicolaou; namely, cornification of the vaginal mucosa during estrus. The effect occurs in the rat and mouse concomitant with certain stages of the estrual cycle (which in these animals has a normal periodicity of from four to six days) but is abolished by ovariectomy. The injection of extracts of liquor folliculi into castrated mature rats was found to induce these changes, which could be detected by microscopic observation of the vaginal smear; when positive, there was replacement of the leukocytes normally present, first by nucleated and later by non-nucleated epithelial cells. The method was later standardized by Doisy and his co-workers and has since been used in the assay of Theelin. It was found that multiple injections of a given minimal quantity of the aqueous preparations of Theelin would produce estrual changes, whereas a single injection of the total amount failed in this respect. The Allen-Doisy method therefore utilized the multiple injection technic. In the more recent Doisy modification of this test, which followed the work of Coward and Burn discussed later, the induction of the vaginal estrous effect in 75 per cent of a large number of rats of standard weight is the criterion of activity.

Modifications made by other workers consist in the use of other animals, notably mice, occasionally rabbits; immature uncastrated animals (utilizing opening of vagina as the criterion of activity); different spacing of multiple injections; single rather than multiple injection; different sites of injection; the use of oily rather than aqueous preparations; different time periods elapsing between injection and reading of smear; these and other variations in practically all the possible combinations. The preparations used by different investigators were, of course, of varying degrees of purity and were varyingly contaminated by other possibly active principles.

It is not surprising, in view of these differences, that in only a few isolated instances have workers in separate laboratories been able to agree on the potency of a given preparation and on the relationship between the two most commonly used units: the "rat unit" and the "mouse unit." Where attempts have been made to use identical technics, agreement of results has been better but ordinarily not striking; in one case brought to the attention of the Council, however (E. A. Doisy and Parke, Davis & Company), assays by the Doisy method are said to be checked repeatedly in two different laboratories within a range of ± 20 per cent.

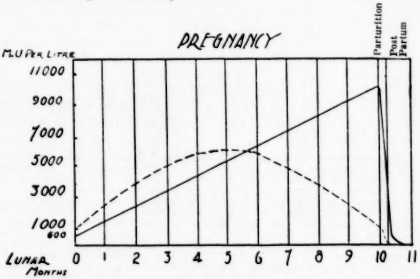

Fig. 2. The excretion of estrogenic substance (solid line) and anterior pituitary-like factors (broken line) in the urine during pregnancy (reproduced through the courtesy of C. Mazer and L. Goldstein).

These factors serve only to emphasize the necessity for more information on absorption, distribution and excretion of Theelin and related products. The problem is made more difficult by the fact that any investigation of these factors must have as its basis an assay method. Consequently, it is unlikely that the early work on this subject will be of more than relative significance. However, in general, by rigid adherence to a given technic, individual investigators have succeeded in obtaining fairly accurately reproducible assay figures for a given product. In fact, Frank has stated that, by meticulous attention to technical detail, accurate results can be obtained with single animals. For this reason, despite the vicious circle involved, significant data should be forthcoming. It is to be hoped that a highly sensitive chemical method may in the future replace the present biologic method.

In the absence of such data, any discussion of the relative value of the assay methods must be based largely on theoretical considerations; definite conclusions are at this time not possible.

The work of Coward and Burn and of Burn and Elphick [68] primarily deserves consideration. These workers found that the variation in the response of animals to injections of estrogenic substance may be as much as 1,000 per cent; in other words, it may take ten times the dose to produce estrus in one animal of a given weight as in another. The basis of this tremendous variability is not understood but it is reminiscent of the unpredictable responses obtained in the early smooth muscle work in which uterine tissue was used. Because of this variability, Coward and Burn decided to use the method established by

66. Corner, G. W.: J. A. M. A. **89:** 1839 (Nov. 26) 1927.
67. Allen, Edgar; Doisy, E. A., and others: Am. J. Anat. **34:** 133, 1924.
68. (*a*) Coward, K. H., and Burn, J. H.: J. Physiol. **63:** 270 (Aug. 8) 1927. (*b*) Burn, J. H.: Physiol. Rev. **10:** 146 (Jan.) 1930. (*c*) Burn, J. H., and Elphick, G. K.: Quart. J. Pharmacol. **5:** 192 (April-June) 1932.

Trevan[69] for biologic assay in general; the percentage of animals in estrus with a given dose was plotted against the dose and a curve constructed. The unit was chosen as that dose which would produce estrus in exactly 50 per cent of animals injected. Once the curve was constructed, future assays were relatively simple. To quote an example of Burn: Twenty rats were each injected with a 10 mg. dose; estrus occurred in nine, or 45 per cent. Reference to the curve already constructed shows that estrus occurs in 45 per cent of animals with 0.94 unit; therefore, 10.6 mg. of this preparation equals 1 unit.

This method appears to have possibilities which merit for it serious consideration, particularly, since by its use D'Amour and Gustavson[70] and Becker and his co-workers[71] have been able to confirm Coward and Burn's results with an agreement surprising in this type of work. One firm (Squibb) has adapted the Coward-Burn curve to a modification of the Allen-Doisy three-injection technic with apparently satisfactory results in the standardization of Amniotin.

With regard to the other factors involved, the following appear to be fairly well established: 1. In rats or mice Theelin or Theelol is much less active in oily solution than in aqueous solution;[68c] in birds, as judged from the feather test, the reverse is true. 2. Multiple injections at intervals increase the activity of a given dose of the aqueous solution[72] but do not materially affect the activity of the same dose in oily solution.[68a] 3. The rat unit and the mouse unit are approximately identical when assayed in oily solution but marked disagreement occurs among the various workers as to the relative values when the aqueous solution is used. The relative weights of the animals appear to be factors when the aqueous solution is injected, but this relationship is by no means constant. The ratios in the literature for the rat unit: mouse unit of the aqueous preparations range generally from 10:1 to 2:1, the most commonly accepted figure being 4:1.

The production of the effects in the genital organs on which the tests are based must necessarily be determined by the availability to the organs in question of the estrogenic substance, i. e., the concentration in the blood stream, and on the capacity of these organs to utilize the substance or to store it pending use. On the latter questions, little definite is known. From the work quoted, it is known, however, that estrogenic activity disappears from the blood stream in a very short time after administration and that the genital tissues are not necessarily involved in this process. It appears, therefore, in consideration of the relative blood supply of these parts, that the genital tract has available only a small portion of any injected dose, even assuming that these tissues remove all the estrogenic substance that reaches them, which appears unlikely. There appears also to be a renal threshold for this substance; at least this apparently exists under certain conditions. On injection of a single large aqueous dose, absorption would be fairly rapid, with a resultant fairly high concentration in the blood stream. If a renal threshold exists, the higher the blood concentration the more likely is the substance to spill over into the urine and become unavailable. Whatever may be the ultimate factors involved in the disappearance of the activity, the evidence indicates that the estrous effect is dependent on a continuous action of the estrogenic substance. A single large dose, unless it is very large, results in but a brief action. When repeated injections are given, the blood stream concentration is of course not as high and the substance is not as likely to appear in the urine—at any rate, the genital tissues receive repeated rather than single stimulation. With oily solutions it is not difficult to understand on this basis why there should be no difference between single and multiple injections; the absorption is at best so slow that continuous action results even from a single injection, and the added depots formed by repeated administration apparently do not add materially to the effect.

There is evidence that the presence of other substances, the characters of which have not been fully studied, enhances the effectiveness[73] of estrogenic preparations. Possibly these are themselves active or modify the rate of absorption. It may be of some value to use the oily solutions clinically, but these generally are not very adaptable to repeated hypodermic administration in the human being (usually olive oil, or some similar vegetable oil is used as solvent).

It appears that the method of assay is of little importance, provided it furnishes an indication of the possible activity of the preparation. It is certain that the multiple injection technic provides the most sensitive test available. That alone should commend it. The single injection technic with either aqueous or oily solutions appears incapable of detecting lower limits of activity. A ratio between the clinical effectiveness and the assay unit, whatever that may be, can and should eventually be established. It appears to be true that workers in different laboratories can check one another with better agreement when using oily than when using aqueous preparations. This is undoubtedly due to the lesser sensitiveness, because a difference in less than 20 Doisy units cannot even be detected by this method. The Council believes that the factors underlying the variability of the Allen-Doisy method should receive careful study rather than that this method should be discarded in favor of one less sensitive. These factors have already been indicated by the work of Frank, and of Fee, Marrian and Parkes, already quoted.

Deterioration of Commercial Products.—A number of reports have appeared in the literature that independent assays have revealed either a complete lack of potency or a diminution of potency from that indicated on the labels of commercial products. The methods of assay are not stated and, therefore, adequate discussion is not possible.

CLINICAL USE OF THEELIN AND RELATED PREPARATIONS[74]

Theelin and related preparations[75] have been used in practically all the special ills the human female "is heir to"; even the male has not escaped. The results in general have been quite disappointing, despite the abundance of case reports available, numbering by now several thousand. In the light of the previous discussion and that which follows, it is not surprising that this should be so; only a very few workers have made any attempt to determine whether in a particular case under consideration a real deficiency exists in the "hormone" which it is proposed to supply, and if such a deficiency is shown actually to occur, whether the particular preparation administered can really remedy the lack.

The work of Frank and of others, already referred to, has demonstrated that the clinical pictures in menstrual and associated disorders furnish little or no definite indication as to the quantity present, in blood or urine, of any of the particular endocrine factors involved in the normal sexual cycle. Herewith are reproduced charts from Mazer and Goldstein[23h] and from Frank,[23d] which indicate in some degree the normal and pathologic variations of these endocrine products in blood and urine.

It cannot be too strongly emphasized that so long as the conditions which determine the concentrations of the sex-endocrine substances in blood and tissues, the sensitiveness of the tissues to these substances, the rates of excretion, and so on, are but little understood, endocrine therapy will remain a hit and miss procedure. This is especially true with the shotgun variety exemplified by the organotherapy of certain commercialized extracts which Frank has so aptly described as "heterogeneous mixtures of inert substances which include all but the hoof and hide of our domestic animals."

F. H. A. Marshall has stated, "The use of [estrogenic substance] is only indicated in cases where there is evidence of a natural deficiency of this substance as with certain types of amenorrhea, or after ovarian extirpation, and, much more problematically, at the time of the menopause. The indiscriminate usage of [estrogenic substance] for other disorders has no basis in physiologic fact, and may justly be stigma-

69. Trevan: Proc. Roy. Soc., series B **101:** 481, 1927 (cited from Burn).
70. D'Amour, F. E., and Gustavson, R. G.: J. Pharmacol. & Exper. Therap. **40:** 485, 1930.
71. Becker, T. J.; Mellish, C. N.; D'Amour, F. E., and Gustavson, R. G.: J. Pharmacol. & Exper. Therap. **43:** 693 (Dec.) 1931.
72. Marrian, G. F., and Parkes, A. S.: J. Physiol. **67:** 389, 1929.
73. Dodds, E. C.: Tr. Am. Gynec. Soc. **56:** 134, 1931.
74. Pratt, J. P., and Allen, Edgar: J. A. M. A. **86:** 1964 (June 26) 1926. Novak, Emil, ibid. **90:** 339 (Feb. 4) 1928. King, J. T., Jr., and Patterson, Ellen, ibid. **91:** 1423 (Nov. 10) 1928. Council Report, ibid. **91:** 1193 (Oct. 20) 1928. Dodds, E. C., and Robertson, J. D.: Lancet **1:** 1390, 1930. Campbell, A. D., and Collip, J. B.: Canad. M. A. J. **22:** 219 (Feb.) 1930. Novak, Emil: J. A. M. A. **95:** 1225 (Oct. 25) 1930. Gardiner-Hill and Smith: Lancet **1:** 464, 1931. Morse, A. H.: Yale J. Biol. Med. **3:** 397 (May) 1931. Hamblen, E. C.: Endocrinology **15:** 184 (May-June) 1931. Kincaid, H. L.: Texas State J. Med. **27:** 313 (Aug.) 1931. Novak, Emil, and Hurd, G. G.: Am. J. Obst. & Gynec. **22:** 501 (Oct.) 1931. Hamblen, E. C.: Virginia M. Monthly **58:** 509 (Nov.) 1931. Frank, R. T.: J. A. M. A. **97:** 1852 (Dec. 19) 1931. Gerhardt, L., abstr. ibid. **98:** 2033 (June 4) 1932. Kurzrok, R., and Ratner, S.: Am. J. Obst. & Gynec. **23:** 689 (May) 1932. Geist, S. H., and Spielman, F., ibid. **23:** 692, 701 (May) 1932. Hamblen, E. C.: South. M. & S. J. **94:** 339 (June) 1932. Werner, A. A.: Proc. Soc. Exper. Biol. & Med. **29:** 1142 (June) 1932. Hirst, J. C.: J. M. Soc. New Jersey **29:** 574 (July) 1932. Kurzrok, R.: Endocrinology, **16:** 361, 366 (July-Aug.) 1932. Novak, Emil: South. M. J. **25:** 856 (Aug.) 1932. Mazer, C., and Goldstein, L.: Clinical Endocrinology of the Female, Philadelphia, 1932. Allen, Edgar, editor: Sex and Internal Secretions, Baltimore, Williams and Wilkins Company, 1932. Kauffmann, C.: Zentralbl. f. Gynäk. **57:** 42 (Jan. 7) 1933. Werner, A. A., and Collier, W. D.: J. A. M. A. **100:** 633 (March 4) 1933.
75. While other preparations, in particular Amniotin (Squibb), have been found in experimental and in clinical use apparently to produce effects comparable to those of the crystalline Theelin, all such products have been classed here under the generic term "estrogenic substance." This is not intended as reflection on the potency or possible usefulness of such products.

tized as quackery." [75a] As will be noted from the data presented in this report, even the conservative indications suggested by this competent investigator have not yet been fully substantiated in actual clinical practice.

The respective rôles played by the various endocrine factors in menstruation is not clear, nor in fact is the actual mechanism of menstruation known. The recent work on this subject, as quoted, indicates that the process is a resultant of the complex interaction of a number of endocrine factors. Blood and urine assays furnish some idea of the relative concentrations in body

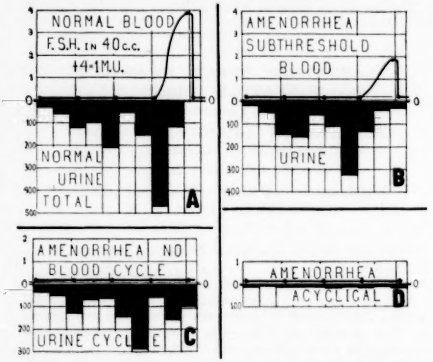

Fig. 3.—Graphs of specimens of blood and of urine showing curve of estrogenic substance in the blood samples (40 cc.), as well as total mouse units excreted in the urine: *A*, normal fertile woman shown for comparison; *B*, amenorrhea (or sterility) with subthreshold blood cycle, and fairly normal urine cycle; *C*, amenorrhea without blood cycle but with urine cycle; *D*, acyclic amenorrhea (reproduced through the courtesy of R. T. Frank [29d]).

fluids of estrogenic and prepituitary factors, as compared with the normal; but even with this information, which in itself is by no means complete, attempts at replacement therapy have generally failed. Many observers have emphasized the necessity for cyclic variations in the treatment in attempts to reproduce the natural concentration curves; somewhat better results have been claimed for this method; but even here, where definite effort has been made to treat the problem with a certain rationality, the benefit received by the patients has not been convincing.

A few clinicians, too few, unfortunately, have attempted to rule out the psychic factors in this problem.[76] Where this has been done, the results indicate that the chief benefit furnished the patient has been psychogenic.

Mazer and Goldstein believe that estrogenic substance in adequate dosage is useful in the treatment of certain cases of genital hypoplasia of not too long standing, of selected cases of amenorrhea and "primary" dysmenorrhea and for the relief of the vasomotor symptoms of the menopause; but here also the results are not completely convincing. In surgical or radiation castration, estrogenic substance can induce uterine bleeding if the treatment is started early enough or if the dosage is large enough; but this is not cyclic (except in the cases of Werner and Collier, reported below). Certain amenorrheic patients can be made to bleed by injection of Theelin; just what benefit such patients derive from the bleeding alone is highly questionable.

The results obtained in the menopause have been variable; benefit has been reported by some workers, but this has been no better than others have obtained with nonspecific treatment.

The work of Kunde and her co-workers and that of Haupstein emphasize the necessity for great caution in the clinical use of estrogenic substance. The daily injection into immature dogs of from 25 to 800 rat units for six to seventeen weeks resulted in relatively sclerotic ovaries less than one-half the size of those in control dogs, anterior hypophyses much smaller, and posterior hypophyses much larger than normal, and markedly hyperplastic thyroid together with other changes of a less serious nature. Similar changes in the ovaries of immature and mature mice have been reported by Haupstein following the repeated injection of large doses.[77]

The findings of Lacassagne on the incidence of spontaneous carcinomas in mice, quoted above,[53a] may possibly be of significance in this connection (although the limited number of observations and the absence of suitable control data with the oil used as solvent, renders this questionable). Evidence of deleterious effect from the clinical administration of estrogenic substance is not conclusive, but the possibility deserves serious consideration, particularly if the large doses more recently employed clinically should come into common usage.

The question of adequate therapeutic dosage remains also a moot point. Marrian and Parkes [78] have pointed out that the unit dosage which produces the estrous response used for assay in mice is insufficient to produce the full response characteristic of normal estrus; the latter requires at least 200 times the unit assay dosage. They assume, therefore, that a quantity of about 200 mouse units is produced by the animal at each estrus. This is probably an unwarranted assumption, since no definite relationship has been shown to exist between the natural output and the amount required to produce an equivalent effect when injected. Marrian and Parkes suggest that if, on a weight for weight basis, an equivalent amount is produced by the human being during the corresponding stage of the cycle, 400,000 mouse units would be required for complete substitution therapy. Recently, C. Kaufmann [74] and Werner and Collier [74] have reported the use of large doses of estrogenic substance in surgically castrated women. Kaufmann injected in a 22 year old patient, 5 years after ovariectomy, 10,000 to 20,000 mouse units a day for 25 days to a total of 300,000 to 320,000 units, followed by a total of 90 rabbit units of corpus luteum factor (progestin) during a period of 6 days; bleeding ensued for 68 hours from an endometrium of the menstrual type. Werner and Collier reported four similar cases in which daily injection of 200 to 400 rat units of Theelin over a period of 89 to 93 days resulted in repeated uterine bleeding during the treatment; the endometrium, however, was of the interval type. Other physiologic effects, including the subjective response, were similar to those occurring in the normal cycle (these latter also were noted in a fifth patient, similarly treated, in whom the fundus of the uterus had been extirpated). Similar but not such striking effects had been reported by Mazer and Goldstein.

In the light of present-day evidence, the anterior pituitary-like [79] and the corpus luteum preparations appear to offer more promise of therapeutic usefulness than the estrogenic preparations. By comparison with the reports published on the latter, those on the use of luteinizing preparations in functional uterine hemorrhage indicate a fairly high percentage of successful treatment.

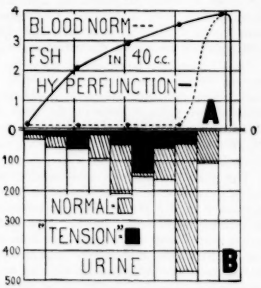

Fig. 4.—Graph showing the concentration curves of estrogenic substance in blood, and total output in urine (mouse units): *A*, puberty and preclimacteric bleeding; broken line indicates normal curve, solid line "hyperfunction"; *B*, total urine output: normal (shaded); and "hypertension" (solid black) due to underexcretion (reproduced through the courtesy of R. T. Frank [29d]).

Theelin has been used with some success in hemophilia. Birch [52] has treated thirty-five cases, and other reports [80] have

75a. Marshall, F. H. A.: Brit. M. J. **2**: 232 (Aug. 6) 1932.
76. Dodds, E. C.: Am. J. Obst. & Gynec. **22**: 520 (Oct.) 1931. Frank, Novak and others.[74]
77. Kunde, M. M., and others: Proc. Soc. Exper. Biol. & Med. **22**: 122 (Nov.) 1930; Am. J. Physiol. **95**: 630 (Dec.) 1930. Haupstein, P.: Endokrinologie **8**: 169, 1931.
78. Marrian, G. F., and Parkes, A. S.: J. Physiol. **69**: 372, 1930.
79. Novak, Emil, and Hurd, G. G.: Am. J. Obst. & Gynec. **22**: 501 (Oct.) 1931.
80. White, C. E.: J. Oklahoma M. A. **25**: 304 (July) 1932. Kimm, H. T., and Van Allen, C. M.: J. A. M. A. **99**: 991 (Sept. 17) 1932.

appeared since her preliminary work. Birch claims better results with extracts of whole ovary than with Theelin alone and considers the latter as of value chiefly during actual hemorrhage. The precise evaluation of the endocrine factors in hemophilia therefore remains to be made in the future.

R. T. Frank,[81] whose experience with estrogenic substance has been quite extensive, states: "While such products as thyroid substance, insulin and parathyroid produce striking and concordant results in appropriate cases, the opposite applies even to the few potent extracts used in the genital sphere. . . . Our hopes have been dashed because of the fact that the potent [estrogenic substance] does not cause the anticipated therapeutic results. This is fully explained since we recognize that this now purified product acts solely on the tubular tract, and according to competent testimony, when given in large doses over long periods, eventually causes sclerosis of the ovaries." Again, he states: "I think that faith cures and Christian science could produce as good results. I must confess that, after having faithfully and continuously worked with [estrogenic substance] for more than twenty-five years, I am forced to acknowledge that this drug has given no therapeutic results."

Mazer and Goldstein state:[82] "In our enthusiasm for hormonal therapy we must not forget that the constitutional symptoms of the menopause often yield to hygienic and dietetic measures, and to such sedative drugs as bromides and barbital derivatives, and we must not likewise forget that the condition is transitory and self limiting."

The prolonged clinical administration of Theelin can produce certain definite effects; but, as Frank has pointed out, these are not the desired effects: some enlargement of the uterus, with endometrial hyperplasia, a sense of fulness in the pelvis; occasionally uterine bleeding; some enlargement of and a sense of fulness in the breasts. Of these, the uterine bleeding alone can be said to approach the desired therapeutic result; but what effect the bleeding per se has on the health of the individual, aside from the psychic benefit derived therefrom, cannot be answered definitely at this time. The psychic response, i. e., subjective improvement, has been attained to the same degree when the Theelin injections have been intermitted with those of physiologic solution of sodium chloride or other inactive preparations, and when nonspecific general therapy has been instituted. Consequently, it cannot at this time be said that Theelin has any specific indication in the treatment of menstrual disturbances.

In all fairness, however, it must be admitted that the subjective response incident on Theelin therapy may well be real. The difficulty arises in evaluating in some satisfactory manner the psychic state of the patient. To date, even with the data furnished by the careful, if necessarily limited, work of Werner and Collier, the evidence must be considered inconclusive.

The place of Theelin and related products in gynecologic therapy remains for the future to decide. Great caution is necessary in the use of these preparations and greater caution in making deductions from it. The indiscriminate use is likely to do more harm than good, not only because of the effect of the preparations themselves but also because general therapeutic measures intended to aid the organism in restoring its own equilibrium are likely to be neglected.

The Council believes that the future of endocrine therapy in the sexual sphere appears quite promising. But it is not surprising in view of the short time that has elapsed since the introduction of active preparations commercially, that little should be known about their therapeutic possibilities. Enthusiasm in this case has in large part seriously interfered with clinical judgment; the clinical use has kept far ahead of the laboratory data; controlled observations have been few indeed. It is time to call attention to the fact that most of the basic facts should first be worked out in the laboratory before they are tried in the clinic.

The Council will undertake further consideration of preparations of the female sex "hormones" as additional studies on the applications of these substances become available, and as the indications for and limitations of their use become more clearly defined.

81. Frank, R. T.: J. A. M. A. **97**: 1852 (Dec. 19) 1931; S. Clin. North America **12**: 310 (April) 1932.
82. Mazer, C., and Goldstein, L.: Clinical Endocrinology of the Female, Philadelphia, 1932, p. 426.

Committee on Foods

REPORTS OF THE COMMITTEE

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

PLANTATION BRAND HAWAIIAN PINEAPPLE (Sliced)
(Standard Quality; Vacuum Packed) Dole 2
PLANTATION BRAND HAWAIIAN PINEAPPLE (Crushed)
(Standard Quality) Dole 2
UKULELE BRAND HALF SLICES HAWAIIAN PINEAPPLE
(Vacuum Packed) Dole 3

Manufacturer.—The Hawaiian Pineapple Company, Ltd., San Francisco.

Description.—"Dole 2" or "grade 2": This grade includes sliced, crushed fruit and tidbits as does dole 1. The material is graded 2 because it is less evenly cut and less uniform in color than is grade 1. The fruit is packed in concentrated pineapple juice syrup (20 per cent sugar).

"Dole 3" or "grade 3": This grade comprises broken slices packed in concentrated pineapple juice syrup (20 per cent sugar).

Manufacture.—See this section for Paradise Island Brand Hawaiian Finest Quality Pineapple (THE JOURNAL, April 8, 1933, p. 1106).

Analysis (submitted by manufacturer).—

	per cent
Moisture	83.4
Ash	0.5
Fat (ether extract)	0.1
Protein (N × 6.25)	0.3
Reducing sugars as invert	6.3
Sucrose (copper reduction method)	6.6
Crude fiber	0.3
Carbohydrates other than crude fiber (by difference)	14.5
Titratable acidity as critic acid	0.9
pH	3.9

Calories.—0.7 per gram; 17 per ounce.

Vitamins and Claims of Manufacturer.—See these sections for Paradise Island Brand Hawaiian Finest Quality Pineapple.

OSCAR MAYER'S GERMAN WIENERS
(Casings Artificially Colored)

Manufacturer.—Oscar Mayer & Company, Packers, Chicago, Ill., and Madison, Wis.

Description.—Wiener sausage prepared from cured pork and beef meat, spiced, smoked and cooked. The casings are artificially colored. The product is U. S. inspected and passed by the Department of Agriculture.

Manufacture.—Top quality sausage beef bulls and hog muscle tissue with some attached fat prepared in the company's plant are used. The spice ingredients include oleoresins and certain essential oils.

The beef, admixed with definite quantities of sodium nitrate, sodium nitrite, salt and water is spread in pans and cured for three days.

The sausage meat contains green shoulder pork admixed with definite amounts of the prepared beef, to which are added the aforementioned curing ingredients in proper proportions. Spices and enough water to give the sausages the proper consistency are added. In no case does the finished product contain more than 10 per cent moisture over that of the raw material (a regulation of the United States Bureau of Animal Industry).

The sausage meat is stuffed by hand by air pressure into clean and tender sheep gut casings. The sausages are linked five inches long, hung on smoke-sticks, washed with water, and placed in a cooler to cure, after which they are thoroughly

smoked at a temperature of 43 C. or higher. Hardwood sawdust and gas fuel furnish the smoke and heat. The smoked sausages are cooked in water containing a small amount of vegetable color for twelve minutes at 82 C., are water-chilled, and are held over night in a cooler before packing. The sausages may be eaten cold or after heating; they need not be boiled. The cooking is sufficient to kill any trichinae that may be present.

The sausages are banded with yellow bands for identification and packed in cartons by girls who disinfect their hands in dilute sodium hypochlorite solution each half hour. The Bureau of Animal Industry regularly tests the product for moisture, nitrites and other possible adulterants.

Analysis (submitted by manufacturer).—

	per cent
Moisture	58.6
Ash	2.4
Fat (ether extract)	26.3
Protein (N × 6.25)	12.6
Reducing sugars as invert	0.0
Sucrose	0.0
Crude fiber	0.05
Starch	0.0
Carbohydrates other than crude fiber (by difference)	0.05

Calories.—2.9 per gram; 82 per ounce.

Claims of Manufacturer.—May be eaten either hot or cold.

JAY-BEE FISHEL'S AYRSHIRE MILK BREAD

Manufacturer.—J. B. Fishel's Bakery, York, Pa.

Description.—A milk bread made by the sponge dough method (method described in THE JOURNAL, March 5, 1932, p. 817) prepared from flour, milk, sucrose, salt, yeast, shortening, malt syrup, and a yeast food containing calcium sulphate, ammonium chloride, sodium chloride and potassium bromate.

Analysis (submitted by manufacturer).—

	per cent
Moisture (entire loaf)	32.5
Ash	2.2
Fat	3.7
Protein (N × 6.25)	11.3
Crude fiber	0.3
Carbohydrates other than crude fiber (by difference)	50.0

Calories.—2.8 per gram; 80 per ounce.

Claims of Manufacturer.—Conforms to the United States Department of Agriculture definition and standard for milk bread.

RED ELEPHANT HARD WHEAT FLOUR (Matured, Bleached)

Manufacturer.—Fant Milling Company, Sherman, Texas.

Description.—A "long patent" hard wheat flour; bleached.

Manufacture.—Selected hard wheat is cleaned, washed, tempered, scoured and milled by essentially the same procedures as described in THE JOURNAL, June 28, 1932, page 2210. Chosen flour streams are blended and bleached with a mixture of benzoyl peroxide and calcium phosphate (1 part to 50,000 parts of flour) and nitrogen trichloride (one-ninth ounce per 196 pounds of flour).

Claims of Manufacturer.—The flour is designed for commercial baking uses.

STROEHMANN'S MILK BREAD (SLICED)

Manufacturer.—Stroehmann Brothers Company, Harrisburg, Pa.

Description.—A milk bread made by the sponge dough method (method described in THE JOURNAL, March 5, 1932, p. 817) prepared from patent flour, water, sweetened skimmed condensed milk, lard, yeast, salt, butter, dry skim milk, malt syrup and a yeast food mixture of calcium acid phosphate, ammonium sulphate, sodium chloride, potassium bromate, potassium iodate and corn starch.

Analysis (submitted by manufacturer).—

	per cent
Moisture (entire loaf)	38.0
Ash	0.7
Fat	3.0
Protein (N × 6.25)	12.1
Crude fiber	0.3
Carbohydrates other than crude fiber (by difference)	45.9

Calories.—2.6 per gram; 74 per ounce.

Claims of Manufacturer.—A milk bread conforming to the United States Department of Agriculture definition and standard.

1. BUTTER CUP BRAND WHITE SYRUP
2. CONSOLATION BRAND WHITE TABLE SYRUP
3. DEERWOOD BRAND WHITE SYRUP
4. DILLON'S RED LABEL BRAND CRYSTAL WHITE SYRUP
5. FAIRWAY BRAND WHITE TABLE SYRUP
6. FAIRWAY BRAND WHITE TABLE SYRUP
7. FAIRWAY BRAND WHITE TABLE SYRUP
8. GLICK BRAND CRYSTAL WHITE SYRUP
9. HARVEST HOME BRAND CRYSTAL WHITE TABLE SYRUP
10. N. J. C. PURE FOOD BRAND FANCY WHITE SYRUP
11. OZARK BEAUTY BRAND FANCY WHITE TABLE SYRUP
12. PORTAGE BRAND CRYSTAL WHITE SYRUP
13. RED RIBBON BRAND CRYSTAL WHITE SYRUP
14. SAMOS BRAND WHITE CRYSTAL SYRUP
15. SCHILLING'S NICOLET CRYSTAL WHITE SYRUP
16. BYERLY TROPHY BRAND WHITE SYRUP
17. USEMORE BRAND WHITE TABLE SYRUP
18. WHITE HOUSE BRAND FANCY TABLE SYRUP

(85 per cent Corn Syrup, 15 per cent Rock Candy Syrup)

Packer.—D. B. Scully Syrup Company, Chicago.

Distributors.—

1. Tindall, Kolbe & McDowell Co., Milwaukee.
2. New York Store Merc. Co., Cairo, Ill.
3. The Copps Company, Stevens Point, Wis.
4. J. S. Dillon and Sons Stores Company, Inc., The Yellow Front Cash Food Stores, Hutchinson, Newton, Winfield, Great Bend, Dodge City, Larned, Kan.
5. Des Moines Wholesale Grocery Co., Des Moines.
6. Twin City Wholesale Grocer Co., St. Paul and Minneapolis.
7. Wood County Grocery Co., Wisconsin Rapids.
8. Glick Mercantile Co., Pittsburg, Kan.
9. Jett & Wood Merc. Co., Wichita, Kan., and Lamar Colo.
   Jett & Wood Central Merc. Co., Hutchinson and Liberal, Kan.
10. Northern Jobbing Co., Chicago and St. Paul.
11. Pocahontas Grocery Co., Pocahontas, Ark.
12. Portage Wholesale Co., Portage, Wis.
13. Woodward Wholesale Grocery Co., Woodward, Okla.
14. Samos Wholesale Grocery Co., Cleveland.
15. Frank C. Schilling Co., Green Bay, Wis.
16. J. A. Byerly Co., Inc., Owosso, Mich.
17. Service Grocer Co., Detroit.
18. Plumb & Nelson Co., Manitowoc, Wis.

Description.—These syrups are the same product as the accepted D. B. Scully White Crystal Syrup; table syrup, corn syrup base (85 per cent) with rock candy syrup (15 per cent) (THE JOURNAL, April 15, 1933, p. 1174).

NEW WAY FLOUR (BLEACHED)

Manufacturer.—Texas Star Flour Mills, Galveston, Texas.

Description.—An "all purpose" hard winter wheat patent flour; bleached.

Manufacture.—Selected hard winter wheat is cleaned, scoured, tempered and milled by essentially the same procedures as described in THE JOURNAL, June 18, 1932, page 2210. Chosen flour streams are blended, and bleached with nitrogen trichloride (⅛ oz. per 196 pounds) and with a mixture of calcium phosphate and benzoyl peroxide (1 part to 50,000 parts of flour).

Claims of Manufacturer.—This flour is designed for bread baking.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 29, 1933

PROPHYLAXIS OF OPHTHALMIA NEONATORUM COMPULSORY IN ILLINOIS

The application to the eyes of new-born infants of silver nitrate or other approved prophylactic for the prevention of ophthalmia neonatorum will become mandatory in Illinois, July 1, under an act recently approved by Governor Horner. The act amends the present law, which provides only for giving information and advice concerning this disease to parents and for investigating cases after they develop.

Last year a similar bill passed the general assembly of Illinois. Then vociferous opposition by Christian scientists, followed by Attorney General Carlstrom's opinion that the bill was unconstitutional, apparently led Governor Emmerson to veto it. This year Attorney General Kerner submitted to Governor Horner a masterly, well reasoned opinion. True, he expressed some misgivings concerning the constitutionality of such an act in Illinois, but he pointed out at the same time that an act passed by the general assembly is to be regarded as constitutional until the contrary is demonstrated beyond a reasonable doubt. The Supreme Court of Illinois, according to Attorney General Kerner's opinion, has tended to confine the exercise of the police power of the state within limits narrower than those conceded in other states and by the Supreme Court of the United States. Governor Horner, however, called attention to the fact that similar legislation had been enacted in other states with apparent benefit, that the constitutionality of such legislation had never been attacked, and that the constitutionality of the present act could not be determined unless he approved the act; accordingly, he approved it.

From a medical point of view there is abundant basis of fact to support the constitutionality of this act under the criterion of constitutionality deduced by Attorney General Kerner from the decisions of the Illinois Supreme Court. "Throughout all of these Illinois cases," says the attorney general, "runs the thought that a valid health police regulation, affecting personal and property rights, safeguarded under the constitution, cannot be predicated upon a condition that does not exist but the existence of which is merely assumed or suspected." Not by the wildest stretch of the imagination can any one assert that the conditions that called forth the enactment of this legislation did not or do not exist and that they are merely assumed or suspected. The gonococcus,. which causes by far the largest number of cases of ophthalmia neonatorum, is one of the most widely distributed of all known pathogenic germs, and pathogenic cocci of other kinds are certainly not restricted in distribution. They have their habitat in the birth passages of many women who are entirely innocent of wrong-doing and utterly ignorant of their presence. The fact that many women are free from such germs is not to the point. Legislation for the protection of the health of the people must be based on the condition of the people as a whole and adapted to their needs. To base such legislation on individual cases and to adapt it to the needs of individual persons is impracticable. It is impracticable in the present instance because the circumstances attending childbirth and the time available for effective prophylaxis after the child is born preclude the determination by a midwife or attending physician with reasonable certainty whether or not the mother is the carrier of infective organisms.

The constitutionality of this legislation for the protection of individual infants and of the public against the hazards of ophthalmia neonatorum and against the lifelong handicaps and expense of defective vision, including even total blindness, should never have been attacked. The protection afforded by the law will do no harm to a child whose eyes are not infected; it will prevent infection in those who might be subjected thereby to permanent blindness. More and more, enlightened legislators and judicial authorities are realizing the real responsibilities of the state in matters affecting the protection of the health of the child.

MILK VS. WINE

Certain American newspapers[1] have recently featured special foreign correspondence alleging that French physicians, "following the well known practice at Vichy, are prescribing more and more the moderate drinking of wine instead of milk for patients suffering from gastric or intestinal troubles." It is further reported that "one of the eminent physicians who are leading the antimilk campaign in favor of wine" regards it as a duty to inform the public about the physiologic advantages of wine. These statements, which have been widely circulated at a moment when the repeal of the Eighteenth Amendment is being discussed in every home, are already promoting numerous inquiries to physicians. It seems peculiarly unfortunate that the problem should be raised in this country at a period

1. For example, the New York Times, April 8, 1933.

when much effort continues to be expended in the attempts to promote a more liberal use of what has been termed "our most nearly perfect food," milk.[2] In a recent issue of THE JOURNAL, for example, Bernheim[3] discussed the calcium problem of the American dietary and arrived at the conclusion that unless milk or cheese is included it would as a rule be "exceedingly difficult to fill the calcium need, since inordinately large amounts of other foods and water would have to be ingested, quantities far beyond the capacity of the normal individual."

The physiologic properties of wines are fairly well known. To what extent alcohol, which occurs in these fermented beverages in quantities ranging commonly from 8 to 20 per cent, is to be ranked as a possible food need not be debated at this time. From the standpoint of its caloric contribution in alcohol alone, a pint of wine of 10 per cent alcoholic strength would supply more than 300 calories. To this is added the varying amounts of sugar and "extract" in solution. Thus the food fuel is by no means negligible. Alcohol in this amount is likely to represent something more than a possible source of energy. It is not devoid of effects that are described either as physiologic or pharmacodynamic, depending on the point of view of the interpreter. The press reports, however, are not content with these familiar aspects! They report the startling allegation that wine also "is an antiseptic which kills cholera microbes. . . . Red wines kill the typhoid fever microbe in two hours. Dry wines kill it in twenty minutes." The colon bacilli also are reported to be the victims of the destructive action of such wines. Bacteriologists will, we are confident, be quite astounded by such claims of germicidal potency; while physiologists will wonder how alcohol can be induced to remain long enough in the alimentary tract to exercise this surprising germ-destroying function—particularly as it is so rapidly absorbed, even from the stomach. The French reports refer further to certain radioactivity, which "has not yet been entirely studied." This sounds like the familiar hoax of radioactive waters, which has reached the zenith of its conjuring power in this country. A well known American investigator once found that the radioactivity of some of the vaunted waters approximated that of unextolled sewage.

"Times have changed," so the press report further states, "because today, at Vichy, doctors no longer prescribe milk for their patients, but wine." Doubtless wine may have a place in the regimen of certain persons, though it continues to be proscribed in the United States. But it would be a step backward to permit exceptional and extreme circumstances — and particularly the doubtful recommendation of pseudoscience — to menace the growing appreciation of the value of milk in the American dietary. Enthusiasts have called milk the modern elixir of life. It is not necessary, however, to deal with such superlatives in assigning to milk a dietary—and often a dietotherapeutic—rôle that even the choicest of vintages of the art of fermentation can never hope to rival.

2. Crumbine, S. J., and Tobey, J. A.: The Most Nearly Perfect Food—The Story of Milk, Baltimore, Williams and Wilkins Company, 1930.

3. Bernheim, Alice R.: Calcium Need and Calcium Utilization, J. A. M. A. **100:** 1001 (April 1) 1933.

THE FEMALE SEX HORMONES

Until recently, therapy employing so-called female sex hormones was limited largely to the use of desiccated ovarian products and various extracts without demonstrated value.[1] These were employed empirically with the hope that they might do good. Today the physician has available preparations of demonstrable potency in animals and of possible usefulness in human beings. Two, isolated in crystalline form, have been given the nonproprietary designations theelin and theelol.[2]

Elsewhere in this issue appears a comprehensive analysis by the Council on Pharmacy and Chemistry of the status of female sex endocrine therapy, particularly with estrogenic preparations. In few branches of physiologic research has experimental work progressed as rapidly as in this field, but clinical observations have not kept pace. Unfortunately, many of the products were submitted to uncontrolled clinical observations; inevitably this reacted to the discredit of endocrine therapy in ovarian and related disorders. A recent series of studies, published in THE JOURNAL, appears to have been carefully executed and promises stimulus to the therapeutic use of estrogenic preparations. Werner and Collier[3] report that daily injection of theelin in five surgically castrated women over periods of from eighty-nine to ninety-three days resulted in repeated uterine bleeding during the treatment. In addition, such benefits as alleviation of symptoms of the menopause were noted. The cervix increased in vascularity; the endometrium showed hyperplasia to the normal intermenstrual but not to the premenstrual phase, and the breasts enlarged. Subjectively, improvement occurred in all the patients; indeed, libido was said to have increased in four. Obviously, all these results require extensive confirmation.

As indicated by the report of the Council, the evidence does not warrant extensive routine application to therapeutics of the results thus far achieved. Whether or not uterine bleeding per se, or the associated phenomena, are essential or even beneficial to the well being of women has not been established. In surgical and radiation castration and in the natural menopause, the beneficial effects seem to resolve into psychic improvement. If such subjective improve-

1. Desiccated Ovarian Preparations for Oral Administration Omitted from N. N. R., J. A. M. A. **94:** 1997 (June 21) 1930; Injectable Ovarian Preparations Omitted from N. N. R., ibid. **98:** 402 (Jan. 30) 1932.

2. Theelin and Theelol, editorial, J. A. M. A. **97:** 33 (July 4) 1931; Theelin—and the Technic of Introducing New Drugs, ibid. **97:** 1541 (Nov. 21) 1931.

3. Werner, A. A., and Collier, W. D.: The Effect of Theelin Injections on the Castrated Woman, J. A. M. A. **100:** 633 (March 4) 1933.

ment is shown later to be constant and inseparably associated with the physical changes, the question of adequate dosage and the hardship associated with daily injections over indefinite periods require consideration.

Research with estrogenic substances, as the Council's report brings out, has been hampered by the confusion resulting from inability to compare the potencies of preparations used in different laboratories. Recently, however, the Health Organization of the League of Nations has undertaken to establish an international standard for such products.[4] The standard preparation is to consist of crystalline material of the hydroxy-ketonic structure (theelin), made by combination of samples from various countries. It will, of course, take time for the work of the League's committee to reach consummation; but the action is a commendable step in the direction of greater comparative accuracy.

Current Comment

ESSENTIAL FATTY ACIDS

In 1929, G. O. and Mildred M. Burr [1] announced that in experimental animals given a ration extremely poor in fat but otherwise adequate there occurred retardation of growth together with other typical symptoms. Not only were the symptoms alleviated by giving a few milligrams of fat but the cure was brought about by the administration of either of the two unsaturated fatty acids linoleic and linolenic acids. The glycerides of the common saturated fatty acids were ineffective.[2] Apparently the necessary unsaturated fatty acids cannot be synthesized by the organism. These observations served to place linoleic and linolenic acids in the category of indispensable dietary factors along with the essential amino-acids, the vitamins and certain mineral elements. Supporting evidence [3] was later brought forth showing that the syndrome was cured by the liquid fatty acids from coconut oil, by linoleic acid, and by the fatty acids of rice and corn starches. It was further stated that only those acids with two or more double bonds were effective in this respect. Subsequent studies [4] indicated that in butter and in tung oil there were undetermined fatty acids which were essential in nutrition. The general thesis of the existence of indispensable fatty acids has not gone unchallenged. At least one of the symptoms—the dermatitis of the tail—has been said to be nonspecific.[5] The question has been raised as to why the liver, with its ability to desaturate fatty acids, does not produce linoleic and linolenic acids from the corresponding saturated fatty acids.[6] Further, the unsaturation of the fatty acids of the tissue phospholipids in rats on a fat-poor diet is of the normal order of magnitude.[7] On the other hand, in a recent report by Evans and Lepkovsky,[8] experiments are described which indicate that the total body fat of animals grown on an adequate ration contains the indispensable fatty acids, whereas that from animals consuming a fat-free diet does not contain these dietary essentials. It is pointed out, however, that the efficacy of the fatty acids from the body fats of the various groups of animals is not parallel to the degree of unsaturation, which fact again raises the question as to the specificity of linoleic and linolenic acids. Experience has shown that the requisite quantity of certain dietary essentials is so small that it might well escape ordinary methods of analysis. The solution of the problem of the indispensability of fat in the ration may therefore depend finally on the refinements of chemical technic.

4. Doisy, E. A.: Science **77**: 344 (April 7) 1933.
1. Burr, G. O., and Burr, Mildred M.: J. Biol. Chem. **82**: 345 (May) 1929.
2. Burr, G. O., and Burr, Mildred M.: J. Biol. Chem. **86**: 587 (April) 1930.
3. Evans, H. M., and Lepkovsky, Samuel: J. Biol. Chem. **96**: 143, 157 (April) 1932.
4. Burr, G. O.; Burr, Mildred M., and Miller, E. S.: J. Biol. Chem. **97**: 1 (July) 1932.
5. Hume, Eleanor M., and Smith, Hannah H.: Biochem. J. **25**: 300 (number 1) 1931.
6. Eggleton, P.: Science Progress **26**: 19, 1931-1932.
7. Sinclair, R. G.: J. Biol. Chem. **96**: 103 (April) 1932.
8. Evans, H. M., and Lepkovsky, Samuel: J. Biol. Chem. **99**: 231 (Dec.) 1932.

THE "LIFE CYCLE" OF THE TUBERCLE BACILLUS

Mellon and his co-workers [1] of the Western Pennsylvania Hospital have recently reported the results of the application of modern single cell methods of bacterial culture to a study of the "life cycle" of the tubercle bacillus. Starting with the classic acid-fast phase of the avian tubercle bacillus, the Pittsburgh investigators found that this familiar clinical type may "dissociate," "mutate" or "degenerate" into minute non-acid-fast cocci. Certain of these cocci show demonstrable nuclei. The nucleated cocci apparently conjugate, the male nucleus migrating into the female cytoplasm. The resulting fertilized female micro-organism divides, first into a non-acid-fast diplococcus, afterward into a non-acid-fast tetrad. This tetrad eventually breaks up into individual cocci, which are now without demonstrable nuclei. The resulting sexually regenerated non-nucleated cocci may germinate into non-acid-fast diphtheroids. These in turn may give rise to acid-fast cocci, which in time usually ripen into the acid-fast bacilli of classic morphology. Such pleomorphic phases of the tubercle bacillus have been previously reported by Miller [2] and numerous other investigators. Mellon, however, is the first to interpret the observed diplococcus and tetrad phases as the result of sexual conjugation. With numerous other pathogenic bacteria, variations in antigenicity or immunochemical specificity have been demonstrated in the different pleomorphic stages. In certain cases, vaccines and antiserums prepared with one bacillary "variant" or "dissociate" are wholly inert against a second morphologic "mutant" of the same culture. Whether or not a similar pleochemism takes place with the tubercle bacillus has not yet been established.

1. Mellon, R. R.; Richardson, R. D., and Fisher, L. W.: Proc. Soc. Exper. Biol. & Med. **30**: 80 (Oct.) 1932. Lindegren, C. C., and Mellon, R. R., ibid. **30**: 110 (Oct.) 1932.
2. Miller, F. R.: J. Exper. Med. **56**: 411 (Sept.) 1932.

Association News

MEDICAL BROADCAST FOR THE WEEK

American Medical Association Health Talks

The American Medical Association broadcasts on Tuesday and Thursday from 9:15 to 9:20 a. m., Chicago Daylight Saving Time, which is one hour faster than Central Standard Time, over Station WBBM (770 kilocycles, or 389.4 meters).

The subjects for the week are as follows:

May 2. Food Advertising Popularity.
May 4. Boys and Girls.

There is also a fifteen minute talk sponsored by the Asssociation on Saturday morning from 9:45 to 10 o'clock over Station WBBM.

The subject for the week is as follows:

May 6. Overweight.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Twenty-Ninth Annual Meeting, held in Chicago, Feb. 13 and 14, 1933

(Continued from page 1260)

DR. T. J. CROWE, Dallas, Texas, in the Chair

THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES

FEBRUARY 14—MORNING

The Philosophy of Medical Licensure

DR. H. M. PLATTER, Columbus, Ohio: The fundamental duty which we, as executives, owe to the profession is that we shall give recognition only to well prepared graduates of reputable medical schools who practice ethical medicine. Boards of licensure must closely supervise licensees and institute proceedings for suspension or revocation of licenses of individuals who are guilty of transgression. I can bear testimony that after honest effort to enforce a medical practice act which has been held constitutional the prosecution of cultists has proved of little lasting benefit. My conviction is that most of this effort is wasted and that practice by unlicensed individuals will continue regardless of how much is expended to eliminate it.

Our department holds hearings quarterly to supervise and control the practices of men holding our licenses. We make in a year about 500 investigations and convict approximately 100 individuals who violate our medical practice act. The records will show that many of those convicted escape with a minimum fine or suspended fine and continue their practices owing to indifference of the courts and the general disregard on the part of all people for regulation and law observance. A certain amount of prosecution and investigation will be necessary if we adhere to the American idea of control of cultism. But in all fairness to the executives it should be understood by medical men, health officers and medical educators that cult elimination is impossible, particularly if we include Christian science among the cults, where it rightfully belongs.

I agree with most of the conclusions arrived at by the Commission on Medical Education, but I dissent from the idea that licensure should be passed on to graduates from approved medical schools because this practice is followed in most countries. I dissent also with the idea that to boards of licensure must be delegated *all* of the effort to enforce medical practice acts. If we could, I would advise a liberal repeal of statutes which cannot be enforced or which visit additional requirements on the qualified man and substitute therefor an agreed on minimum standard. Unfortunately, cults have gained considerable legal recognition in the several states. For the good of licensure, all such provisions should be repealed.

Dental Licensure Problems

J. V. CONZETT, D.D.S., Dubuque, Iowa: Dentistry is a young profession, not having yet attained its first century. The first dental college was organized in Baltimore in 1839, this making the Baltimore College of Dental Surgery the oldest dental college in the world. It was organized by Drs. Hayden and Harris, because the Baltimore Medical College refused to place a chair of dentistry in that institution. Dentistry was looked on as a trade, or at best as a prosthetic art, ministering to the esthetic values of the mouth and teeth, and dentistry was refused recognition as a branch or part of the healing profession. I do not in any way bring this as an accusation against medicine, for I give place to no man in my admiration for that profession. Now dentistry is a separate profession, with its own colleges, degree and literature. This fact, which is peculiar to America, has made American dentistry the recognized leader of the dental profession of the world.

After the institution of the first dental college, others rapidly followed. As there were no limiting laws to regulate the profession, these colleges were a law unto themselves. The entrance requirements were nil. There was a chaotic condition in dental education. It early became apparent that some regulation of the practice of dentistry was necessary; therefore the various states began to place laws on their statute books making it illegal to practice without the authority of the state as defined by the law. It will be remembered that the dental schools in the early years had no generally accepted minimum entrance requirement or rules governing promotion and graduation, therefore the product of the various schools was decidedly irregular. Dental colleges grew rapidly. Some of them were little better than advertising offices catering to the public and, at the end of a stipulated term, furnishing diplomas to the students. This condition became so distressing that the National Association of Dental Examiners in 1909 advised the appointment of an educational council, appointed five men from its membership to act as a nucleus of such a committee, and suggested that the National Dental Association and the American Association of Dental Teachers appoint like committees to join in the organization of a joint educational council. The Dental Educational Council of America was formed with five men from each of the parent organizations as members. Attempts were made to draft minimum requirements of entrance, promotional and graduational status. The better schools gladly accepted the suggestions but, not having the necessary authority, the council found its work decidedly uphill. When the war came, it was found in an attempt to organize a dental department in the Surgeon General's Office that there was so low a professional ability in the product of some schools that a diploma from a school, or even a certificate from a state board, did not mean that the applicant was competent to practice his profession in the army. Surgeon General Gorgas then called on the Dental Educational Council of America to make a survey of the schools, grade them as A, B and C, and said that he would accept the graduates of the A and B schools and give them commissions in the army but that the product of the C schools would have to take their places in the ranks. This gave the council the power it needed, and immediately the low grade schools began to make a rush to make good and attempted to attain the minimum requirements as suggested by the council. This made possible the elimination of many of the poor and commercial schools, and during the progress of the war sincere attempts to improve were made by those schools. Then the Carnegie Foundation made the survey of dental education, which was followed by the grading of all schools in the United States as A, B and C, a potent factor in the elevation of the teaching conditions in the various schools. As a result, most of the dental colleges in the country now carry an A rating. The weak schools have been eliminated, and many that needed assistance have merged, made university connections, and in other ways advanced their positions educationally so that now the educational status of the dental colleges of the United States is very good. That there is still room for improvement, no one will deny.

The one drawback to dentistry at present is that a man legally capable of practicing in one state is not so qualified in an adjoining or distant state. The medical or the dental degree should carry with it the authority to practice that profession in any state in the Union. Now that the colleges have been standardized, there is a great need that the state boards should be standardized. Some time ago the Dental Educational Council of America attempted to find some method whereby such a plan might be put into effect, but after mature study it was unable to find a point of entrance for such a

survey. The alternative and the ideal is a central examining board that would be able to conduct examinations for all candidates for the profession and have their decisions recognized in all the states of the Union. This attempt has been made and there is now the National Board of Dental Examiners, composed of fifteen members selected from the three national dental organizations, the American Dental Association, the National Association of Dental Examiners, and the American Association of Dental Teachers. The difficulty with the National Board of Dental Examiners is that the various state boards have not the legal right to accept the national board's certificates; but it is hoped that that difficulty will soon be overcome by proper legislation. With such a board the work of the teaching staffs in the dental colleges might be lightened, for such a board might take charge of the final examinations in the colleges in lieu of the final examinations on the part of the college authorities. The diploma and the certificate of the national board would thus harmonize and be recognized throughout the United States.

The state board of dental examiners is the only authority recognized by the state laws; consequently, a national board could operate only through the cooperation of the state board. It and it only would be the final authority and could at will accept or reject the findings of the national board in all or any specific case. This is the case now and must be in the future until some method can be devised whereby a national law could take the place of state laws in all health matters. It might be premature to discuss the matter of the regulation of the practice and conduct of those already in practice; but in view of the fact that the large majority of physicians and dentists begin to retrogress the moment their diplomas are placed in their hands and in view of the tremendous importance of the ability and honesty of the members of the health professions to the health of the people, it would seem wise to adopt some plan of supervising the fitness of the men in the professions to continue their administrations to public health.

I confidently expect that the physician or the dentist of the future will have to give evidence in some way, to properly constituted authorities, of his ability to continue efficiently his ministrations to the public in a health program. In our hands is placed the responsibility of the health and happiness of the people. If we can adopt a program whereby we can unite in the education, examination and continued edification of the members of our professions we shall not only advance the interests of all of the members but gain the confidence of the public in a manner that has never yet been attained.

Training for Practice Abroad

DR. WILLIAM D. CUTTER, Chicago: It is my purpose to deal with the regulations governing medical education and licensure in Great Britain and northern Ireland, France, Germany, Austria, Italy and Switzerland.

In France and Germany particularly opportunities for practical experience such as are in this country provided by the clinical clerkship and the internship are not granted to American students. The completion of the required course of study, therefore, even though attested by a university degree, cannot be regarded as equivalent to training given in approved medical colleges in the United States and Canada. Furthermore, it has been shown that in continental Europe it is practically impossible for an American citizen to qualify for licensure. This fact may well be brought to the attention of those representatives of other nationalities who may be inclined to protest against the formulation of rules designed to protect the standards of medical practice in this country.

Foreign Medical Graduates in New York State

DR. HAROLD RYPINS, Albany, N. Y.: Prior to the war, the number of foreign graduates coming to New York State was not very great and in general the graduate of any reputable European medical faculty was accepted for admission to the New York medical licensing examination on the basis of much less evidence as to the quality of his professional training than that required of a graduate of an American or a Canadian school. Since the war, the number of such foreign graduates has gradually increased and the members of the board of medical examiners have found it increasingly difficult to evaluate the medical knowledge of these foreign applicants. In 1931 I compiled statistics showing the relative achievements of 6,462 American and foreign graduates admitted to the New York medical licensing examination during the six-year period 1925-1930, inclusive. At that time there were 5,026 American graduates (including Canadians), constituting 77.7 per cent of all the candidates, among whom there were 9.1 per cent of failures. In contrast to this, there were 1,436 foreign graduates, comprising 22.3 per cent of all the candidates, of whom there were 44.5 per cent of failures. These data were presented at a joint meeting of the New York board of medical examiners and the council of deans of New York State medical schools. On the request of these bodies, who felt that this problem was national, I presented the data to the Council on Medical Education and Hospitals at its meeting in Philadelphia in June, 1931. As a result, on the recommendation of the Council on Medical Education and Hospitals, the House of Delegates passed a resolution that the Council on Medical Education and Hospitals make a classification of foreign medical schools where students of American citizenship are in attendance, along the lines applied in the classification of American medical colleges.

In the Aug. 29, 1931, issue of THE JOURNAL, the Council reported a survey of American students studying medicine abroad, reports having been received from 98 of the 165 foreign schools questioned. This survey revealed that there were 630 such students (exclusive of Canada). A similar survey conducted by the Council and published in THE JOURNAL, Aug. 17, 1932, showed 1,174 students (exclusive of Canada) in foreign medical schools for the year 1931-1932, or almost double the number for the previous year. In addition, information was received that more than 500 more New York students were planning to emigrate during the summer and fall of 1932, so that by this time there are between 1,500 and 2,000 American boys studying medicine abroad.

During the last eight years, the number of foreign-born graduates has steadily diminished, probably owing to the operation of the immigrant quota. The number of foreign-born candidates, 126, admitted to the New York medical licensing examination in 1932 is less than half of those admitted, 294, in 1925, but the proportion of failures among foreign-born students has increased from 47.7 per cent in 1925 to 62.7 per cent in 1932, having reached a high point of 74 per cent in 1930.

By far the larger group consists of American students studying in Europe, only a few of whom have completed their studies and returned to take the state licensing examinations. A far-reaching effect will be accomplished by the recognition on the part of European educational authorities that this country is not at present satisfied with the medical education of Americans in Europe and that it expects a European authority to maintain the same standards for American students in reference to admission and graduation requirements now maintained in the best American and European schools qualifying for medical practice here and abroad. Now that the attention of the European authorities has been directed to this problem, there is every reason to believe that they will seek out a solution to the problem which will satisfy all concerned.

The problem of the licensure of medical students trained in Europe must ultimately be considered, to a certain extent at least, in reference to the definite selection and limitation of the number of physicians trained for and licensed to practice medicine throughout the United States.

DISCUSSION

DR. W. H. G. LOGAN, Chicago: Dr. Conzett pointed out that the first dental school in the world was created some ninety years ago. Medical education began in the United States seventy-five years before, yet medicine did not come to a preliminary standard of high school education until 1910. Six years after that time, dentistry came to the same high school standard. At present there are thirty-eight dental schools in the United States, fourteen of them requiring two years of collegiate preliminary education and the remainder one year of collegiate preliminary education. There has been some discussion of the possible change in the trend of dental education over into that of medicine, but, with the exception of a single school aggressively in favor of the taking of dental education into that of medicine and requiring the medical

degree before the further training of dentistry, the remainder of the thirty-eight favor the continuation of the training of dentists as an independent profession; they also favor a more thorough understanding of the definite relation that exists between mouth health and general disease. I believe that standardization in dental education will be effected on the minimum standard now set up for medicine; namely, two years of collegiate training, with an ultimate four years of dental training. The best dental schools are carrying their senior students into a general hospital, that they may find patients who show the relation between oral and systemic disease. In addition, dental interns in the hospital and interns in oral surgery are being added. I am surprised that this body has not demanded that more than seventeen states in the United States should have an intern year before an examination is granted. Dental teachers and those governing this problem would not think that a dentist could be trained by precept and by observation. I ask that some influence be created to extend to the remainder of the forty-eight states. The dental men of this country feel that medicine should care for its own problems, and we as dentists wish to join you in that movement. We believe that thereby will the public be best served.

DR. HENRY M. FITZHUGH, Baltimore: I am in accord with the main points made by Dr. Platter, first, that it is the duty of the boards to select for license only men who are well qualified to take the resources of science and medicine to the public. I agree with his idea that it is no part of the duty of organized medicine to be fighting the cults. It probably is part of our duty to prosecute quacks. We find that it is difficult in Maryland to do much. The people are rather indifferent.

DR. J. GURNEY TAYLOR, Milwaukee: It seems that the discussion centers on what should be done with the cults. I think, with Dr. Fitzhugh, that it is wise for us to attend to our own knitting. The enforcement of the medical practice acts is before our boards at all times and has caused serious embarrassment. Up to a short time ago, Wisconsin had its investigator functioning under the medical board. He was transferred and put under the board of health, since which time much better results have been secured. In the last six months of 1932 there were eighty-nine cases tried, and eighty-two convictions, approximately 90 per cent, were secured.

DR. H. M. PLATTER, Columbus, Ohio: We instituted about 125 cases and had 100 convictions. We had about fifteen cases that were dismissed, so our proportion runs in line with yours, about 80 per cent.

DR. TAYLOR: The question of carefully supervising the licenses is a large order for the secretary of a medical board. With men scattered over the state it is hard to follow up the acts of those who are already licensed. There is one part of the law in Wisconsin that has worked out successfully: when a physician is convicted of a crime in the course of his professional work, the court submits its findings to the board, and the board has no chance to do anything except cancel his license.

DR. T. J. CROWE, Dallas, Texas: All violations?

DR. TAYLOR: No, criminal. In the minor types of misdemeanor, the board must institute its own civil procedure in the courts.

DR. CLAUDE A. BURRETT, New York: The problem is one of determining what shall be done with those of our people who cannot receive educational advantages in this country and go abroad. It is apparent that it is really not an educational problem so much as it is a problem of selection. The present problem of the foreign medical graduate in America is largely centered in New York City. It may be difficult for one not in the midst of New York life, and especially its educational life, to appreciate fully what the medical educational limitations in America have meant to the great number of young men and women in that city who desire a medical education. Our compulsory educational system is turning out thousands of graduates each year. Not only is secondary education compulsory, but higher education in the municipal colleges of New York City is free and great numbers of these students find their way into the city colleges, as well as the other colleges and universities. The result of it is that literally hundreds each year are seeking further training looking toward a life work. The average layman, especially if he is a father of one of these, cannot see why his son or daughter should be turned away from further education in his chosen profession. Fundamentally, then, it is a problem of more adequate educational and vocational guidance and an elevation of the dignity of a wider range of human activities. It is clear that American students receive didactic training under difficult conditions, with little opportunity for clinical observation and no internship in European countries, owing to the fact that it is reserved for citizens of those countries. Since New York examinations are wholly written, I wonder whether these American students would not be able to pass the examination of the New York state board. I feel that the recommendation of Dr. Rypins, that in order to be admitted to the New York board examination one must be a licensed practitioner of the country in which he received his education, is a just one and reciprocal in the matter of distribution of physicians in the various countries. The problem of professional education in America rests on the opportunity that is given in this country for free education through the high schools, and in large cities such as New York and in many of the states for practically free higher education. Our professional schools and their administration are then embarrassed by our American system of free education. Contrary to this, in all the countries of Europe, education must be paid for directly by the individual above the grade schools of those countries. I feel, therefore, that the problem we have before us is more than the simple one of requirement for admission to our schools. It is even more than the question of what we shall do with those who may want to go to European countries. I think we must face directly the problem of our needs for physicians in this country and face it on that basis.

DR. WILLIAM S. LADD, New York: These provisions do not keep any qualified student from going abroad and studying and, if he can fulfil certain qualifications, transferring back to this country. There is provision made for special consideration of well qualified cases. The action, as I understand it, is to correct the abuses that seem to be coming along in the present situation. I am in accord with the regulations and the suggestions that the federation has made in regard to this regulation of foreign medical students.

DR. WALTER L. BIERRING, Des Moines, Iowa: At this time there are changes going on in the French method of medical education. A committee has been appointed, of which Drs. Roussy and Rist are members. Several pamphlets have been published in which they propose changes in the present plan. They are endeavoring to approximate toward the American plan of education. Dr. Rist, who is in this country now, is to meet Drs. Rappleye and Rypins on Thursday and Friday of this week to consider these changes. Their purpose is to have restrictions that will keep out foreign students, except those who are very desirable. They have a great influx of students from Russia that they are anxious to keep out. They want to use these American regulations for that purpose.

DR. I. D. METZGER, Pittsburgh: The secondary schools in our country have brought up lists of applicants not only for medicine but for all other professions. During the last two weeks we had a meeting of the presidents of the boards of Pennsylvania. All these boards are facing the same situation which the medical board is facing; that is, of an unusually large number of candidates. Candidates up to 40 per cent have been flunked in the law examinations. They are deliberately making their examinations so difficult that scarcely one may pass. I am glad to know that medicine is not taking that course. It is not fair to encourage a person to study medicine until he has completed his course and then prevent him from practicing. We must somehow train students of secondary schools to understand that the professions do not hold up quite the bright outlook which they have been led to believe they do.

(To be continued)

The Ketogenic Diet and Epilepsy.—We may say that with the ketogenic diet alone, without special attention to water or mineral metabolism, one third of the cooperative intelligent epileptics can be made free from seizures. The best results are obtained in children and young adults who are just beginning to have seizures. Patients with frequent attacks of long duration respond less favorably.—Pulford, D. S.: The Present Status of the Ketogenic Diet, *Ann. Int. Med.* **6**:797 (Dec.) 1932.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ARKANSAS

Personal.—Recent appointments to the Arkansas Board of Health include Drs. William G. Hodges, Malvern, Wells F. Smith, Little Rock, and Thomas Wilson, Wynne. All three were named for terms expiring in December, 1937.——Dr. Frank Vinsonhaler, dean, University of Arkansas School of Medicine, Little Rock, was recently awarded a medal by Columbia University, New York, for conspicuous service rendered to the university.

Dr. Grayson Appointed State Health Officer.—Dr. William B. Grayson, McGehee, was elected state health officer and secretary of the board of health, April 10. Dr. Grayson, whose appointment will be effective June 13, will replace Dr. Charles W. Garrison, who has served in the position eighteen years. Dr. Grayson was president of the Desha County Medical Society in 1931 and secretary of the society from 1927 to 1931. He is 36 years of age and a graduate of Tulane University of Louisiana School of Medicine, New Orleans.

CALIFORNIA

Health at San Diego.—Telegraphic reports to the U. S. Department of Commerce from eighty-five cities with a total population of 37 million, for the week ended April 15, indicate that the highest mortality rate (18.4) appears for San Diego, and the rate for the group of cities as a whole, 11.1. The mortality rate for San Diego for the corresponding period of last year was 13.8, and for the group of cities, 12. The annual rate for eighty-five cities for the fifteen weeks of 1933 was 12.1, as against a rate of 12.6 for the corresponding period of last year.

Dr. Rosenau's Courses at the University.—Dr. Milton J. Rosenau, professor of preventive medicine and hygiene, Harvard University Medical School, Boston, will give two courses at the summer session of the University of California at Berkeley. One course will deal with elementary epidemiology, the evolution of methods of disease prevention and control based on studies of the history, prevalence, etiology, sources and modes of infection of the principal preventable diseases. The other course, elementary public health, will cover the field of public health in the United States, including a consideration of the causes of death, sickness and disability, the conservation of infant and child health, the home and the industrial environment, the noncommunicable diseases, and the presentation of health instruction.

Society News.—Dr. Arthur Dean Bevan, Chicago, addressed the Los Angeles Surgical Society, March 10, on peptic ulcer. ——Dr. George F. McCleary, retired medical officer of the ministry of health of Great Britain, London, England, addressed the Los Angeles County Medical Association, March 1, on health insurance in Europe.——Karl F. Meyer, Ph.D., of the Hooper Foundation for Medical Research, University of California, San Francisco, addressed a joint meeting of the Hollywood Academy of Medicine and the Southern California Veterinary Medical Association, April 20, on "Diseases Akin to Man and Beast."——The Trudeau Society was addressed in Los Angeles, April 18, by Drs. Charles S. Young, Los Angeles, and John Dunlop, Pasadena, on "Arthrodesis of the Vertebrae for Tuberculous Disease" and "Operative Fixation of Tuberculosis of the Sacro-Iliac Joints," respectively.

DISTRICT OF COLUMBIA

Personal.—Dr. Joel T. Boone, captain, medical corps, U. S. Navy, March 31, terminated his assignment as physician at the White House, which covered a period of more than ten years. He has been assigned to the Naval Medical School at Washington. Later he is scheduled to be chief of medical service aboard the navy hospital ship *Relief*.——Dr. Charles W. Tegge, Washington, was awarded the Silver Star, February 8, for gallantry in action in the Meuse-Argonne, as a lieutenant in the twenty-third infantry, second U. S. Division.

A New Beaumont Society.—An undergraduate medical society has been organized at George Washington University School of Medicine, Washington, in honor of Dr. William Beaumont. One hundred years ago, March 6, 1833, Dr. Beaumont was given the honorary degree of doctor of medicine by George Washington University. It is hoped that the society will encourage individual investigation among medical students. Meetings will be held twice a month, when papers will be presented by members on cases they have been studying or from research of medical literature.

Heart Association Extends Activities.—The Washington Heart Association has taken steps to extend its activities to include preventive measures against heart disease and social service work to patients with heart disease, according to the *Medical Annals* of the District of Columbia. The association has been composed of physicians interested mainly in the scientific study of heart disease. It is now planned to form a board of governors of twenty members, consisting of physicians and laymen. A full time secretary has also been engaged. The death rate from heart disease in Washington is greater than that in any other city in the United States, the report stated. Dr. James A. Lyon is president of the association; Dr. Lewis C. Ecker, vice president, and Dr. James W. Esler, secretary.

FLORIDA

Bills Introduced.—S. 203 proposes that, before any person is permitted to take an examination for a license to practice medicine, osteopathy, chiropractic or naturopathy, he possess a certificate from a state board of credentials, which this bill proposes to create. The certificate must show that (1) he is a person of good moral character, (2) that he has graduated from an accredited high school and (3) that he has in all other matters complied with the educational qualifications required by the practice act under which he seeks a license to practice the healing art. H. 18 proposes to repeal the law creating a board of optometry examiners and regulating the practice of optometry. H. 45 proposes to create a state spinal health research bureau in the state board of health and to create the office of state chiropractic supervisor who is to be charged with investigating and reporting to proper officials all violations of the chiropractic practice act. H. 170 proposes to define chiropody as "the diagnosis, medical, surgical, palliative, and mechanical treatment of ailments of the human foot or leg, except the amputation thereof; and shall include the use and prescription of local anesthetics." H. 215 proposes to authorize the sexual sterilization of certain socially inadequate residents of the state. H. 243 proposes to levy an annual occupational tax on physicians equal to 2 per cent of their gross incomes. H. 372 proposes to grant compensation and medical services to workmen who suffer personal injuries by accident arising out of or in the course of their employment or who contract diseases or infections as natural and unavoidable results from industrial injury. Workmen are not to be permitted to select their own physicians.

ILLINOIS

Bill Introduced.—H. 667 proposes to require every hospital to have on duty at all hours a person licensed to practice medicine in all its branches.

State Medical Meeting at Peoria, May 16-18.—The eighty-third annual meeting of the Illinois State Medical Society will be held in Peoria, May 16-18, with headquarters at the Pere Marquette Hotel, and under the presidency of Dr. John R. Neal, Springfield. Dr. Olin West, Secretary and General Manager, American Medical Association, among others, will address the secretaries' conference, Tuesday morning, on contract practice. Dr. Charles B. Wright, associate professor of medicine, University of Minnesota Medical School, Minneapolis, will deliver the oration in medicine, Tuesday afternoon. Dr. Harry S. Crossen, professor of clinical gynecology, Washington University School of Medicine, St. Louis, will give the oration in surgery, Wednesday morning, on "The Surgeon's Duty in Cancer of the Uterus." There will be symposiums on arthritis, heart disease and industrial hygiene. The following physicians will be included among the speakers:

Frank J. Jirka, director, state department of public health, Springfield, Outlook for Public Health.
Harry S. Gradle, Chicago, Etiology of Ocular Disease.
Harold Swanberg, Quincy, Value of Combined Cholecystography and Liver Function Tests.
Andy Hall, Mount Vernon, Cooperation Between the Health Department and the Local Physicians.
Hymen J. Burstein, Decatur, Pathology of the Urinary Bladder.
Frank Deneen, Bloomington, Fungus Infections of the Lung.
Arthur H. Parmelee, Oak Park, Importance of Roentgenologic Examination of Growing Bones.
Loyal Davis, Chicago, Roentgenology of Intracranial Tumors.
Maximilian J. Hubeny, Chicago, Insurance Aspect of Roentgenologic Cardiology.
Benjamin H. Orndoff, Chicago, Pneumoperitoneum and Surgery in Management of Abdominal Adhesions.
Howard L. Alt, Chicago, Primary Hypochromic Anemia.
Frank Garm Norbury, Jacksonville, Use of Sodium Amytal in Myoclonic Encephalitis.

Chicago

Banquet to Dr. McLean. — Because of his interest in Provident Hospital and in Negro medical education in general, the Cook County Physicians' Association sponsored a testimonial banquet, March 17, in honor of Dr. Franklin C. McLean, acting president of the Rosenwald Fund. Dr. Midian O. Bousfield was toastmaster. Speakers included Judge Albert B. George; Alderman R. R. Jackson; Dr. Nicholas Alfred G. Diggs, president of the physicians' association; Admiral Norman J. Blackwood, medical director of Provident Hospital; Mr. A. L. Jackson, president of the board of trustees of the hospital, and Dr. Paul C. Hodges, professor of roentgenology, University of Chicago. Following Dr. McLean's response, Dr. Carl G. Roberts presented him with an inscribed fountain pen desk set.

Health During the World's Fair.—Precautions are being planned by the Chicago Health Department for health of the visitors to the Century of Progress Exposition during the coming summer. Particular attention will be paid to water and sewage disposal, purity of food and milk, examination of employees, and adequate comfort stations and drinking fountains. The department will have complete control over all other health matters. The fair grounds will be under the same health supervision as the rest of the city. Tourist camping grounds within the city limits will also be under strict supervision, while outside camps will be under the control of state authorities. Tourist camps desiring the sponsorship of A Century of Progress must submit their plans for sanitary facilities and the control of communicable diseases to the health department for approval before any action will be taken by exposition officials. Food handlers have already been examined for communicable disease.

IOWA

State Medical Meeting at Des Moines, May 10-12.—The Iowa State Medical Society will hold its eighty-second annual session in Des Moines, May 10-12, with headquarters at the Hotel Fort Des Moines, and under the presidency of Dr. William W. Bowen, Fort Dodge. Out of state speakers will include the following physicians:

Della G. Drips, Rochester, Minn., Treatment of Functional Menstrual Irregularities in Young Women.
William C. Finnoff, Denver, Tuberculosis in Ocular Disease.
William A. Plummer, Rochester, Diagnosis of Mild and Atypical Cases of Exophthalmic Goiter.
James A. Evans, La Crosse, Wis., Hyperinsulinism: Case Reports and Discussion of Medical and Surgical Treatment.

The address in surgery will be delivered, Wednesday, by Dr. Harry M. Richter, professor of surgery, Northwestern University College of Medicine, Chicago, on "Radical Gastric Surgery in Peptic Ulcer." Dr. David P. Barr, Busch professor of medicine, Washington University School of Medicine, St. Louis, will give the address in medicine, Thursday, on "The Functions of the Anterior Lobe of the Hypophysis." Other physicians on the program will include:

Frederick H. Lamb, Davenport, Agranulocytosis.
George M. Crabb, Mason City, Appendicitis: Its Increasing Mortality.
Clarence L. Heald, Sigourney, How Can the Present Mortality from Appendicitis Be Lowered?
Frederick W. Mulsow, Cedar Rapids, The Perforated Appendix.
William E. Ash, Council Bluffs, Malaria Therapy of Neurosyphilis Other Than Dementia Paralytica.
Harry W. Vinson, Ottumwa, Use and Abuse of Cesarean Section.
Albert A. Schultz, Fort Dodge, Leads in Diagnosis.
Allen C. Starry, Sioux City, Laboratory Technic and the Practice of Medicine.
John E. Brinkman, Waterloo, Ruptured Renal Aneurysm with Complete Recovery After Operation.
Guy T. McCauliff, Webster City, Rupture of Wounds Following Abdominal Operations.
James F. Taylor, Sioux City, Labor Complicated by Misplaced Placenta.
Thomas F. Thornton, Waterloo, Diagnosis and Management of the Toxic Thyroid.
Clarence W. Baldridge, Iowa City, Diagnosis of Hypothyroidism.
Royal A. Becker, Atlantic, Surgical Accidents.
Harold J. McCoy, Des Moines, Rational Viewpoint in Medical Practice.
John E. Rock, Davenport, Intra-Ocular Foreign Body: An Unusual Case Report.
Frank L. Secoy, Sioux City, Retinal Blastoma.
Henry I. McPherrin, Des Moines, Allergy.
Jack V. Treynor, Council Bluffs, Infections of the Zygomatic Fossa.
Ben G. Dyer, Ames, The Running Ear.
Dean M. Lierle, Iowa City, Histology of the Inner Ear.

Dr. Felix A. Hennessy, Calmar, will be the toastmaster at the annual banquet, Thursday evening, when Dr. Bowen will give the presidential address on "The Progress of Medicine." Dr. Charles B. Taylor, Ottumwa, president-elect, and B. J. Price, attorney, Fort Dodge, will also speak. Entertainment will include a smoker, card party and luncheons. The State Society of Iowa Medical Women will hold its thirty-sixth annual meeting, May 10. Dr. Drips will address the society, among others, on "Functional Disturbances of the Menopause."

KENTUCKY

Lectures on Obstetrics. — Dr. James R. McCord, professor of obstetrics and gynecology, Emory University School of Medicine, Atlanta, is conducting a series of seven courses on obstetrics in Kentucky. Dr. McCord lectured at the City Hospital, Louisville, April 3-7, and at Paducah, April 17-21.

Society News.—Dr. James R. McCord, Atlanta, addressed the Jefferson County Medical Society, March 20, on maternal mortality.——Drs. Fred W. Rankin and Edward H. Ray, Lexington, addressed the Harlan County Medical Society, Harlan, February 25, on "Diagnosis and Treatment of Cancer of the Rectum" and "Intra-Urethral Resection of the Prostate," respectively.——Dr. Irvin Abell, Louisville, made an address on diverticulitis before the Campbell-Kenton County Medical Society, Covington, February 16.——Dr. Arthur T. McCormack, Louisville, discussed "Future Prospects of Medicine in the United States" and Dr. Edward B. Willingham, Paducah, "Emergencies in Heart Disease" at the quarterly meeting of the Southwestern Kentucky Medical Association at Mayfield, February 14.——Drs. George W. Bushong, Tompkinsville, and Beverly Douglas, Nashville, Tenn., addressed the Third District Medical Society at Glasgow, February 15, on "The Whole Time Health Unit and the General Practitioner" and "Empyema in Children," respectively.——Dr. Daniel M. Griffith, Owensboro, addressed the Muhlenberg County Medical Society, Central City, February 15, on abscess of the lungs.——Dr. Philip F. Barbour, Louisville, addressed the Lincoln County Medical Society, Stanford, February 14, on rheumatic diseases in children.

MARYLAND

Gift of Books.—A collection of books pertaining to public health, assembled by the late Dr. John S. Fulton, first full time state health officer for Maryland, and executive officer of the state department of health for nearly thirty years, was recently presented to the department's library by Mrs. Fulton. There are more than a hundred volumes in the collection, in addition to pamphlets and charts.

Health Officers' Conference.—The fourteenth annual conference of the health officers and boards of health of Maryland will be held in Baltimore, May 5-6, under the auspices of the state board of health. The conference will bring together health officers, physicians, county commissioners and boards of health, mayors of cities, state, county and local superintendents of schools, public health nurses and others interested in public health activities.

MICHIGAN

Bills Introduced.—H. 474, to amend the osteopathic practice act, proposes (1) to dub osteopaths, physicians and surgeons of the osteopathic school of medicine; (2) to permit licensed osteopaths to practice medicine and perform surgery, without restriction; (3) to require applicants for licenses to be graduates of accredited high schools, to have successfully completed sixty hours of college work and to have graduated from osteopathic schools of medicine accredited by the board; (4) to authorize osteopaths to make and sign birth and death certificates, and (5) to require that osteopaths be permitted to practice in hospitals supported in whole or in part by public revenue. The requirement as to college work is not to apply to students now matriculated in any recognized college of osteopathy. S. 144 proposes to create a department of registration of professions, to assume the functions of the board of registration in medicine, board of osteopathic registration, board of pharmacy, board of registration in chiropody, board of dental examinations, board of registration of nurses, board of examiners in optometry, and other boards for the examination and licensing of various professions. S. 147, to amend the workmen's compensation act, proposes to grant compensation for certain enumerated occupational diseases.

MINNESOTA

Tuberculin Test for Teachers Compulsory.—All teachers in Minneapolis will be required to submit to the Mantoux tuberculin test before the opening of school in September, according to a recent ruling of the board of education. Arrangements will be made by the director of hygiene.

Society News.—Dr. Martin Nordland, Minneapolis, conducted a clinic on goiter before the Hennepin County Medical Society, April 26, and Dr. Owen H. Wangensteen, Minneapolis, spoke on "Recognition and Treatment of Bowel Obstruction." The society was addressed, April 12, by Drs. Arthur E. Smith and Virgil J. Schwartz, Minneapolis, on "Diagnostic Significance of Pupillary Changes" and "Bronchoscopic Problems in General Practice," respectively.

MISSISSIPPI

Scholarships Awarded.—Five scholarships for the study of medicine at Tulane University of Louisiana School of Medicine, New Orleans, available under the Commonwealth Fund's plan of cooperation with the Mississippi State Board of Health and the university, have been awarded. The scholarships provide $100 a month for the students throughout the medical course on condition that they will return to Mississippi for their first three years' practice, serving in communities of not more than 5,000 population. When the five students selected begin the 1933-1934 term at Tulane this fall, Mississippi will have fifteen scholarship students in attendance.

Society News.—The Coahoma County Medical Club was recently reorganized with Drs. Thack G. Hughes, Clarksdale, as president; Carrie Z. Ballard, Dublin, vice president, and Vernon B. Harrison, Clarksdale, secretary.——Dr. Henry G. Rudner, Memphis, Tenn., addressed the East Mississippi Medical Society in Meridian, February 16, on "Symptoms of Colon Dysfunction—Diagnosis and Treatment."——The Homochitto Valley Medical Society recently heard Dr. Lucien S. Gaudet, Natchez, discuss "A Piece of Steel in the Lens of the Eye Removed by Magnet Through the Original Wound" and "Brain Tumor Operation." Dr. Felix J. Underwood, Jackson, also spoke on "The Present State of Public Health."

MISSOURI

Bill Passed.—H. 664 has passed the house and the senate, proposing to make it lawful for licensed physicians to prescribe intoxicating liquors in such quantities and with such frequency and dosage as in their judgment the needs of their patients may require.

Personal.—Dr. James Archer O'Reilly, St. Louis, has been appointed associate professor of orthopedics in the St. Louis University School of Medicine.——The state house of representatives adopted a resolution extending greetings to Dr. Josiah G. Moore, Mexico, on the occasion of his seventieth birthday, January 31; Dr. Moore is a member of the house.——Dr. William G. Patton has been appointed superintendent of St. Louis County Hospital, Clayton.——Dr. Mazyck P. Ravenel, Columbia, has recently been made an honorary member of the Royal Sanitary Institute of Great Britain.

State Medical Meeting at Kansas City, May 1-4.—The seventy-sixth annual meeting of the Missouri State Medical Association will be held at Kansas City, May 1-4, with headquarters at the President Hotel, and under the presidency of Dr. Joseph W. Love, Springfield. According to the preliminary program, guest speakers will include Drs. Charles A. Elliott, Chicago, on "Parenchymatous Hepatic Disease"; Arnold S. Jackson, Madison, Wis., "Diagnosis and Treatment of Diseases of the Thyroid Gland"; Peter C. Kronfeld, Chicago, "Development of the Tear-Searing Operation Up-to-Date," and John Gordon Wilson, Chicago, "Vertigo." Other papers will be presented by the following physicians:

Willard Bartlett, Jr., St. Louis, Renal Complications of Gallbladder Disease.
Marvin L. Bills, Kansas City, Interpretation of Pathological Reflexes.
Frederick B. Campbell, Kansas City, Anorectal Infection: Its Relation to General Medicine.
Oswald P. Falk, St. Louis, Treatment of Cardiac Episodes of Middle Life.
Edward T. Gibson, Kansas City, Narcolepsy.
A. Morris Ginsberg, Kansas City, Gastric Symptoms of Acute Heart Diseases.
Joseph E. Glenn and Cyrus E. Burford, St. Louis, Management of Bladder Diverticula.
Thomas B. Hall, Jr., Kansas City, Enlarging Conceptions of Mycotic Infections of the Skin.
Arthur E. Hertzler, Kansas City, Diseases of the Breast.
Ellery M. Hetherington, Kansas City, Operation for Retroversion of the Uterus and Varicosities of the Broad Ligaments.
Claude J. Hunt, Kansas City, The Bleeding Duodenal Ulcer.
William H. Olmsted, St. Louis, Arteriosclerosis of the Lower Extremities with Special Reference to Treatment of Diabetic Gangrene.
Carl J. Reis, St. Louis, Increasing Significance of Allergy.
Ernest Kip Robinson, Kansas City, Radium in Gynecology.
Joseph Hoy Sanford, St. Louis, Transurethral Prostatectomy: Indications and Limitations.
Daniel L. Sexton, St. Louis, Headaches Associated with Endocrine Disorders.
George H. Thiele, Jr., Kansas City, Symptomatology and Diagnosis of Anorectal Diseases.
August A. Werner, St. Louis, Effect of the Thyroid, the Pituitary and the Gonads on Preadult Development.
Paul V. Woolley, Kansas City, Simplicity in the Treatment of Anorectal Diseases.

In addition to these papers, there will be symposiums on diseases of the liver; gastro-intestinal diseases; diseases of the heart; tuberculosis, and diseases of the eye, ear, nose and throat.

NEBRASKA

District Meeting.—The spring meeting of the Third Councilor District of the Nebraska State Medical Association was held in Beatrice, April 13. A symposium on "Benign and Malignant Lesions of the Cervix and Uterus" was presented by Drs. Harold P. Kuhn, Ferdinand C. Helwig and Edward H. Skinner, Kansas City, Mo. Drs. Edwin Davis and William P. Wherry, Omaha, presented papers on "Prostatectomy and Prostatic Resection" and "Chronic Paranasal Sinus Pathology," respectively. Drs. Adolph Sachs and Benjamin Carl Russum, Omaha, conducted a heart clinic in the evening.

NEW JERSEY

Society News.—Dr. Temple S. Fay, Philadelphia, addressed the Mercer County Medical Society, Mercer, February 8, on "Critical States of Stupor, Coma and Convulsions."——Dr. Douglas Quick, New York, addressed the Morris County Medical Society at New Jersey State Hospital, Greystone Park, February 16, on "Radiation in Cancer."——Dr. Josephine B. Neal, New York, addressed the Union County Medical Society, Summit, February 8, on anterior poliomyelitis. A special meeting of the society was held, February 15, to consider the report of the Committee on the Costs of Medical Care, with Drs. Henry O. Reik, Atlantic City, and James B. Morrison, Newark, secretary of the Medical Society of New Jersey, as speakers.——The maternal welfare committee of the Medical Society of New Jersey reported recently that all counties but three in the state have organized maternal welfare commissions since the committee was established in 1931. Dr. Arthur W. Bingham, East Orange, is chairman of the committee.——Mr. Murray Jenkins, general counsel, United States Fidelity and Guarantee Company, addressed the Essex County Medical Society, Newark, March 23, on "Legal Problems Connected with the Practice of Medicine."——Dr. Earl B. Craig, Philadelphia, addressed the Cape May County Medical Society at its annual dinner, March 14, in Ocean City, on cancer, and Dr. Henry O. Reik, Atlantic City, discussed medical economics.

NEW YORK

New Activities in Westchester County.—The Medical Society of the County of Westchester has recently opened executive offices in White Plains, with James E. Bryan as executive secretary. Publication of the *Westchester Medical Bulletin* was begun in April, with Dr. Henry T. Kelly as editor and Mr. Bryan as business manager. Mr. Bryan is the son of Dr. Joseph H. Bryan, Asbury Park, N. J. Dr. Nellis B. Foster, New York, addressed the society, April 18, on "Problems in the Diagnosis of Diseases of the Liver." Drs. Charles Geschickter, Baltimore, and George T. Pack, New York, spoke, March 21, on "Clinical Aspects of Cancer of the Breast" and "Radiation Therapy of Breast Cancer," respectively.

Society News.—Dr. Charles Gordon Heyd, New York, addressed the Medical Society of the County of Albany, February 15, on "The Changing Order in Medical Affairs." Speakers at the meeting, March 15, were Drs. Frederick C. Conway and Arthur W. Wright, on hypertension, and Joseph L. Holohan, electrocoagulation of the tonsils.——Dr. Morris Rosenthal, New York, addressed the Dutchess-Putnam Medical Society, Poughkeepsie, February 8, on "Compensation Agreement" and Dr. Irving D. Steinhardt of the New York Physicians' Mutual Aid Association, "United to Help Each Other."——Drs. Herman E. Pearse, Jr., Rochester, and MacNaughton Wilkinson, Rochester, addressed the Livingston County Medical Society, Dansville, in January, on "Neoplasms: Their Diagnosis and Treatment" and "Use of Sodium Amytal in Obstetrics," respectively.——The New York State Association of Public Health Laboratories held its annual meeting at the Ellis Hospital, Schenectady, April 26.——Dr. Lawrason Brown was reelected president of the Saranac Lake Society for the Control of Tuberculosis at the annual meeting, March 1.

New York City

Personal.—John Culbert Faries, director of the Institute for the Crippled and Disabled since 1919, has resigned on account of poor health.

Medal Awarded to Professor Sherman.—The medal of the American Institute of Chemists awarded annually for outstanding service to chemistry will be presented to Henry C. Sherman, Ph.D., executive officer of the department of chemistry, Columbia University, at the annual meeting of the institute in May in New York. The award is made in recognition of Dr. Sherman's research on food and his service in the training of chemists. He received his advanced degrees at

Columbia and has been teaching in the university since 1898. His most recent research has been concerned with the effect of diet on longevity, carried out in collaboration with the Carnegie Institution of Washington. For fifteen years he has been associated with the food supply committee of the New York Association for Improving the Condition of the Poor and is chairman of the committee on nutritional problems of the American Public Health Association.

Society News.—At the meeting of the Medical Society of the County of New York, March 27, a symposium on the "Acute Abdomen" was presented by Drs. John F. Erdmann, Frederic W. Bancroft and Charles E. Farr.——Drs. Benjamin V. Derrah and Chester L. Davidson addressed a joint meeting of the Queensboro Surgical Society and the Medical Society of the County of Queens, March 28, on "Value of a Complete Urological Examination in Upper Urinary Tract Pathology" and "Acute Gangrenous Appendicitis with Spreading Peritonitis," respectively.——A symposium on cutaneous cancer was presented at the meeting of the International and Spanish-Speaking Association of Physicians, Dentists and Pharmacists, March 17, by Drs. George Miller MacKee, Douglas Quick, J. Frank Fraser, Ralph N. Tripp and Jacob Wachtel.—— Dr. Bradley L. Coley addressed the New York Surgical Society, April 26, on "Solitary Bone Cyst—the Localized Form of Osteitis Fibrosa Cystica."——A symposium on pelvic measurements was presented at a meeting of the Medical Association of the Greater City of New York, April 17, by Drs. Herbert Thoms, New Haven, Conn.; Henry J. Walton, Baltimore, and William E. Caldwell. Dr. Burrill B. Crohn addressed the association, March 20, on abdominal pain and a symposium on the "acute abdomen" was presented by Drs. Robert F. Barber, Frank Bethel Cross and Alfred L. Loomis Bell.——Dr. Ralph H. Boots delivered the seventeenth afternoon lecture of the New York Academy of Medicine, March 17, on chronic arthritis, and Dr. Marcus A. Rothschild, the eighteenth, March 24, on heart disease.

OHIO

Personal.—Dr. Eldred V. Thiehoff is acting director of the Cleveland Child Health Association in the absence of Dr. Richard A. Bolt, who is to spend a year in Germany. ——Dr. Henry E. Beebe, Sidney, recently celebrated the sixtieth anniversary of his entrance into medical practice. He is 84 years old.——Dr. Merrill F. Steele, Fort Wayne, Ind., has been appointed superintendent of Grant Hospital, Columbus.

Society News.—Drs. Karl D. Figley and Howard J. Parkhurst, Toledo, among others, addressed the Cleveland Allergy Society, March 28, on "Silk Sensitivity, with Special Reference to Atopic Eczema."——Dr. Albert D. Ruedemann, among others, discussed "Extra-Ocular Muscle Imbalance and Its Associated Head Pains" at a meeting of the Cleveland Neurological Society, April 19.——Dr. Albert C. Furstenberg, Ann Arbor, Mich., addressed the ophthalmologic and otolaryngologic section of the Cleveland Academy of Medicine, April 28, at a meeting open to all members of the academy, on osteomyelitis of the skull.——Dr. Russell L. Haden, Cleveland, was the guest speaker at a joint meeting of the Cincinnati Academy of Medicine with the Cincinnati Dental Society, April 10, on "Dental Infection and Systemic Disease." A symposium on poliomyelitis was presented, April 24, by Drs. Merlin L. Cooper, who discussed etiology; Frank E. Stevenson, symptomatology, and John W. McCammon, orthopedic care.—— Dr. James M. Pierce addressed the Cincinnati Obstetrical Society, April 13, on "Treatment of Acute Pelvic Inflammation."——At a meeting of the Logan County Medical Society in Bellefontaine, April 7, Dr. Harold Swanberg, Quincy, Ill., spoke on "Present Status of Radium Therapy."

PENNSYLVANIA

Anniversary Volume of County Society.—The Cambria County Medical Society has issued a special volume commemorating its eightieth anniversary, which was observed at a meeting, Dec. 15, 1932, at the Hendler Hotel, Johnstown. The historical volume bears the name of the society's bulletin, "The Medical Comment." Early records of the society were destroyed in the Johnstown flood of 1889, but the editors have assembled the early history as fully as possible from other sources. Beginning with the first meeting after the flood, June 10, 1889, the minutes of the society up to the first publication of *Medical Comment* in 1917 are printed for the first time. A section is devoted to photographs and biographies and the final section to the minutes of the women's auxiliary, organized in 1925. Drs. George Hay and Joseph J. Meyer, Johnstown, collected the historical material and edited the 350 page volume.

Philadelphia

Appointments at Temple.—Recent appointments to the staff of Temple University School of Medicine include: Drs. Barton R. Young and Wilbur P. Bailey, assistants in radiology; Samuel Lawrence Woodhouse, Jr., Frank M. Dyson and Francis C. Hartung, clinical assistants in medicine; Chester Reynolds and Frank J. Noonan, clinical assistants in obstetrics and rhinolaryngology, respectively; Louis Alexander Soloff, assistant in clinical pathology; Gerald H. J. Pearson, lecturer in pediatrics, and Bradford Green, instructor in obstetrics.

Annual Cancer Course.—The Philadelphia County Medical Society presented its second annual cancer course, April 11-14, with demonstrations at various hospitals and evening meetings and scientific exhibit at the society's building. Hospitals participating were Hahnemann, Jefferson, Graduate, American Oncologic, Philadelphia General, Jeanes, Jewish and Lankenau. Sessions were also held at Temple University Medical School, University of Pennsylvania School of Medicine and Woman's Medical College of Pennsylvania. Addresses at the evening sessions were as follows:

Dr. Joseph McFarland, Factors Constituting Malignancy in Tumors.
Dr. Jonathan M. Wainwright, Scranton, What Has Been Done and What Can Be Done in Cancer Control.
Dr. William H. Woglom, New York, Recent Investigations on Resistance to Transplantable Tumors.
Dr. Warren H. Lewis, Baltimore, Cancer Cells, with motion pictures.

The last evening was devoted to a symposium on recognition and treatment of early lesions and early diagnosis, presented by Drs. Carroll S. Wright, George M. Dorrance, John B. Carnett, Chevalier Jackson, Louis H. Clerf, Henry L. Bockus, Damon B. Pfeiffer, Leon Herman and Catharine Macfarlane.

Society News.—Members of obstetric societies of New York, Philadelphia and Boston held a joint meeting in Philadelphia, April 6, during which clinics were held in various hospitals.——Dr. Vincent D. Vermooten, New Haven, Conn., addressed the Philadelphia Urological Society, March 27, on "Underlying Causes of Ureteral Dilatation and Hydronephrosis Following Transplantation of the Lower End of the Ureter" and Drs. David M. Sidlick, Harold S. Rambo and Abram Strauss, "Treatment of Visceral Syphilis with Acetylarsan." ——Drs. Joseph T. Beardwood, Jr., and Donald M. Pillsbury addressed the Academy of Stomatology of Philadelphia, March 28, on "The Rôle of Dentistry in the Management of Diabetes Mellitus" and "What the Dentist Should Know About Syphilis," respectively.——The program of the Philadelphia County Medical Society, April 26, was presented by Drs. Frederic H. Leavitt, who spoke on "Mental Disease, the Modern Plague"; Frederick William Sunderman, "The Bearing of Recent Studies on the Prevention of Diabetic Coma," and Michael G. Wohl, "A Typical Hyperthyroidism and the Significance of the Basal Metabolic Rate."

RHODE ISLAND

Low Records for Contagious Diseases.—A survey of five contagious diseases in Rhode Island during the period 1928-1932 revealed that death rates for typhoid, diphtheria and scarlet fever were the lowest in the history of the state. The mortality rates for measles and whooping cough also declined in the five-year period, though both diseases reached record-breaking peaks of morbidity in 1932. The survey showed an average of forty-seven cases with six deaths a year for typhoid. Diphtheria declined from 641 cases in 1928 to 260 in 1932, an improvement held to be the result of state-wide immunization. Scarlet fever averaged 1,431 cases, with fourteen deaths a year. For measles the average was 4,925 cases a year, with 34 deaths, and for whooping cough it was 592 cases, with 33 deaths. In 1932 there were 11,330 cases of measles and 975 of whooping cough.

SOUTH CAROLINA

Bill Introduced.—H. 1010 proposes to require hospitals treating members of both the white and Negro races to employ nurses of both races and to prohibit hospitals from allowing a white nurse to render any service to any Negro patient other than to take temperature and to dress incisions in cases of surgical operations.

SOUTH DAKOTA

Dr. Tarbell Honored.—The Watertown District Medical Society had as a guest of honor at its meeting, March 14, Dr. Hervey A. Tarbell, celebrating his fiftieth anniversary in the practice of medicine. Dr. Tarbell received a silver vase bearing his name and the dates of his practice, 1883-1933. Dr. Chester A. Stewart, Minneapolis, made an address on tuberculosis and Dr. August E. Bostrom, De Smet, described the recent typhoid epidemic at Chamberlain.

TENNESSEE

State Medical Election.—Dr. Hiram B. Everett, Memphis, was elected president of the Tennessee State Medical Association at the annual meeting in Nashville, April 13, succeeding Dr. William P. Wood, Knoxville. Vice presidents elected were Drs. Kyle C. Copenhaver, Knoxville; William S. Rude, Ridgetop, and George G. Malherin, Brownsville. Dr. Harrison H. Shoulders, Nashville, was reelected secretary-editor.

Society News.—Dr. John C. Burch addressed the Nashville Academy of Medicine, March 28, on "Treatment of Functional Uterine Bleeding."——Dr. Cecil B. Tucker addressed the Knox County Medical Society, Knoxville, March 14, on "Eastern Type of Rocky Mountain Spotted Fever."——Dr. Daniel R. Thomas, Calderwood, addressed the Blount County Medical Society, April 6, on "Use and Abuse of Nerve Sedatives."——At a meeting of the Chattanooga and Hamilton County Medical Society, April 6, Dr. Henry H. Hampton discussed tumors of the breast.——Dr. Edward M. Fleenor, Johnson City, addressed the Washington County Medical Society, April 6, on angina pectoris.

TEXAS

State Medical Meeting at Fort Worth, May 8-11.—The sixty-seventh annual session of the State Medical Association of Texas will be held in Fort Worth, May 8-11, with headquarters at the Texas Hotel. At the opening general session Dr. John H. Foster, Houston, will deliver the presidential address; Caleb Perry Patterson, Ph.D., chairman of the department of government, University of Texas, Austin, will speak on "Three Roads to Collectivism" and Henry F. Vaughan, Dr.P.H., Detroit, "Medical Participation in Public Health Work." At other general sessions speakers will be:

Dr. Edward H. Cary, Dallas, President, American Medical Association, Is the American Medical Association Essential to the Welfare of the Public?
Dr. Isidore Cohn, New Orleans, Personal Experiences in Gastric Surgery.
Dr. Irving W. Potter, Buffalo, Technic of Elective Version.
Dr. Albert C. Broders, Rochester, Minn., Reiteration and Elaboration of Some Practical Observations and Deductions on Pathology of the Living.
Dr. Frederick A. Willius, Rochester, Minn., Treatment of Congestive Heart Failure.
Dr. Walter L. Treadway, Washington, D. C., The Drug Addiction Situation.

In addition, Dr. Cohn will recount "Personal Experiences in Fractures" as guest of the section on surgery; Dr. Potter will address the section on gynecology and obstetrics on "Abdominal Cesarean Section"; Dr. Willius, the section on medicine and diseases of children, on "Adiposity of the Heart"; Dr. Broders, the section on surgery, on "Grading of Cancer: Its Relationship to Metastasis and Prognosis"; Dr. Vaughan, the section on public health, on "Immunization and Diphtheria Control," and Dr. William A. Wagner, New Orleans, the section on eye, ear, nose and throat, "Histopathology of Nonspecific Sinusitis." The president's reception and ball will be held at the Texas Hotel Tuesday evening, May 9. Golf tournaments will be arranged at the Rivercrest Country Club. The Texas Dermatological Society, the Texas Neurological Society, the Texas Radiological Society and the Texas Railway Surgeons Association will hold their annual meetings, and a conference of county and city health officers will be held, May 8.

WISCONSIN

Bill Introduced.—A. 817 proposes that if a child is so advanced in intra-uterine age that if delivered, it might live after separation from its mother and grow into the ordinary activities of life, a right of action shall exist in its favor for any injury wantonly or negligently inflicted on its person at that intra-uterine age or in favor of its personal representative in the case of its death from any such injury.

Increase in Heart Disease.—Provisional mortality figures for 1932 show that deaths from heart disease in Wisconsin gave a death rate of 218.5 per hundred thousand of population, in comparison with a rate of 202.9 for 1931. The rate is said to be the highest ever recorded by the state health department. A marked increase in influenza also occurred, 28.6 for 1932 in comparison with 18.7 for 1931. Tuberculosis, on the other hand, showed a decline from 48.7 in 1931 to 45.1 for 1932. The infant mortality rate was estimated provisionally at about 46 per thousand live births, as compared with 52.9 in 1931. The death rate from diarrhea and enteritis under 2 years of age was 6.9, the lowest ever reported. Incomplete reports of deaths amounted to 30,046 and of births, about 53,000.

Society News.—Drs. Solomon Strouse, Chicago, and Edmund H. Mensing addressed the Milwaukee County Medical Society, March 10, on "The Clinical Laboratory in Relation to the Clinic" and "Peritonitis—The Pathologic Physiology Involved in Its Treatment," respectively.——Dr. Sanford R. Gifford, Chicago, addressed the Milwaukee Academy of Medicine, March 21, on "Ocular Findings in General Diseases." Drs. Herman L. Kretschmer, Chicago, and Arthur A. Schaefer addressed the academy, February 21, on "Transurethral Resection of Bladder-Neck Obstruction" and "Inheritance and Significance of Blood Groups," respectively.——Dr. Pol N. Coryllos, New York, addressed the University of Wisconsin Medical Society, March 13, on "The Bronchial Obstruction Syndrome in Pulmonary Diseases."——Drs. Stanley J. Seeger, Milwaukee, and Patrick R. Minahan, Green Bay, addressed the Brown-Kewaunee County Medical Society, February 21, on carcinoma and medical economics, respectively.——Dr. Joseph Brennemann, Chicago, addressed the Racine County Medical Society, Racine, February 16, on "Treatment of Empyema in Children" and Drs. Eugene T. McEnery, Chicago, and John A. Bigler, Highland Park, Ill., "Diagnosis of Tuberculosis in Children by X-Rays."——Dr. Frank Smithies, Chicago, discussed "Diseases of the Stomach and Gallbladder" at a meeting of the Fond du Lac County Medical Society, Fond du Lac, March 8.

GENERAL

Impostor Impersonates Physician.—Dr. Sanders Lewis Christian, medical officer in charge, U. S. Marine Hospital, Norfolk, Va., has reported that a swindler has recently impersonated him, cashing checks in his name. No description of the man was available except that he was said to be elderly and somewhat pompous. He was reported to be in El Paso, Texas, about the middle of March, where he registered at the Hussmann Hotel and joined the El Paso Club.

Training for Teachers of the Near-Blind.—Special training for teachers of children with seriously defective eyesight will be offered during this summer at Western Reserve University, Cleveland, University of Chicago, and Teachers College, Columbia University, New York, the National Society for the Prevention of Blindness announces. "Sight-saving" classes are now a part of the educational system in 119 communities in the United States. Further information may be obtained from the society, 450 Seventh Avenue, New York.

Epidemiologic Numbers.—The *American Journal of Hygiene* announces that henceforth it will publish two epidemiologic numbers each year, in May and November. This action is taken in order to fill a need caused by the discontinuance of the *Journal of Preventive Medicine* with the last issue of 1932. Edwin O. Jordan, Ph.D., professor of hygiene and bacteriology at the University of Chicago, who was editor of the *Journal of Preventive Medicine*, will be associate editor for the epidemiologic numbers of the *American Journal of Hygiene*.

Mothers' Day and Maternal Mortality.—In its third annual Mothers' Day campaign, the Maternity Center Association is directing attention this year to the need for improved maternity care. With this objective, medical societies, women's clubs and welfare organizations will cooperate in the observance of Mothers' Day, May 14. The association states that recent statistics indicate a slight improvement in maternal mortality. Material for local campaigns will be provided without charge by the Maternity Center Association, 1 East Fifty-Seventh Street, New York.

International Organization on Heart Disease.—At a meeting of the Educational Committee for Study and Combat of Heart Disease in Würzburg, Germany, March 7, which was attended by both German and foreign cardiologists, an international committee for study and combat of heart disease (Internationale Komitee zur Erforschung und Bekämpfung der Herzkrankheiten) was formed. The purpose of the international committee is to promote uniformity in nomenclature and cooperation in the study of the natural history of heart disease. The Heart Committee of the New York Tuberculosis and Health Association, of which Dr. Ernst P. Boas is chairman, was offered the leadership in the undertaking. The first meeting will be held in 1934, probably in Germany.

Tuberculosis Scholarships.—Two competitive scholarships for study at the Benito Mussolini Institute at Rome have been placed at the disposal of the International Union Against Tuberculosis by the Italian Fascist National Federation Against Tuberculosis. They provide for a stay of eight months for young physicians who wish to improve their knowledge of the disease. The work undertaken will be subject to agreement between the director of the institute and the candidate. The scholarships will be awarded by the executive committee at a meeting in July. Names of candidates, with a record of their

qualifications, age and professional experience should be sent to the secretariat of the International Union Against Tuberculosis, 66 Boulevard St.-Michel, Paris, not later than July 1.

Society News.—The sixteenth annual meeting of the American Association for Thoracic Surgery will be held in Washington, D. C., May 9-11, with headquarters at the Willard Hotel, and under the presidency of Dr. George P. Muller, Philadelphia. The preliminary program includes the following speakers: Drs. Richard H. Overholt, Boston, "Selective Surgical Collapse for Lung Abscess"; Howard L. Beye, Iowa City, "Operative Mortality from Thoracoplasty in Pulmonary Tuberculosis—Study of Six Cases"; Jay Arthur Myers, Minneapolis, "Collapse Therapy and the Ambulatory Patient"; Louis H. Clerf, Philadelphia, "Carcinoma of the Bronchus"; Julian A. Moore, Asheville, N. C., "Closed Intrapleural Pneumolysis: A Critical Review," and Maurice M. Berck, New York, "Surgical Significance of Some Aspects of the Gross Pathology of Pulmonary Tuberculosis."

Impostor Arrested for Worthless Checks.—*California and Western Medicine* recently reported that George Stanley Paris, who has posed as a physician in several states, had been arrested in Los Angeles on a charge of passing worthless checks in Oakland. Paris's activities were described in THE JOURNAL, Sept. 3, 1932, page 841, after he had attempted to swindle physicians and hospitals in Bristol, Tenn., and in New York City. Records of the California State Board of Medical Examiners show that Paris, who uses such variations of his name as George I. Paris, George Samuel Isaacman and Samuel Paris, has served prison sentences in California and Missouri. At different times he has claimed graduation from Stanford University and the University of Illinois. In New York he said that he had served internships in two hospitals in Hollywood, Calif., and that he was licensed to practice medicine in California. He did serve as an intern at Windsor Hospital, Glendale, Calif., which is not an accredited hospital, according to records of the California state board. No record has been found to show that the man ever attended a medical school or received a license to practice medicine.

National Academy of Sciences.—The National Academy of Sciences held its annual meeting in Washington, D. C., April 24-26. Among speakers who discussed medical subjects were:

Dr. Walter B. Cannon, Boston, Recent Studies on Chemical Mediation of Nerve Impulses.
Dr. Harvey Cushing, Boston, Basophilic Activation of the Hypophysis and Its Bearing on Certain Diseases.
Dr. Charles R. Stockard, New York, Gene Constitution and Endocrine Quality in Determining Growth Reactions.
Wilbur W. Swingle, Ph.D., Princeton, N. J., Studies on the Function of the Adrenal Cortical Hormone and the Cause of Death from Adrenal Insufficiency in Dogs.
Dr. Florence R. Sabin and Kenneth C. Smithburn, New York, Cellular Reactions to Lipoids from Acid-Fast Organisms.
John R. Murlin, Ph.D., Rochester, N. Y., Gluconeogenesis from Fat.
Carl Voegtlin, Ph.D., Herbert Kahler and Richard H. Fitch, U. S. Public Health Service, Action of the Parenteral Administration of Sugars on the Hydrogen Ion Concentration of Normal and Malignant Tissue in Living Animals.
Dr. Herbert M. Evans, Berkeley, Calif., The Anterior Hypophyseal Substance Which Synergizes with Prolan.
Elmer V. McCollum, Sc.D., H. D. Kruse, Sc.D., and Elsa R. Orent, Sc.D., Baltimore, Effects of Deprivation of Magnesium in the Animal Body.

Association for the Study of Goiter.—The preliminary program of the annual meeting of the American Association for the Study of Goiter at Memphis, May 15-17, has been announced. Headquarters will be at the Peabody Hotel. Dr. Henry S. Plummer, Rochester, Minn., will give the presidential address. The scientific program will include the following physicians as speakers:

George E. Beilby, Albany, N. Y., Exophthalmic Goiter in Children.
Willard O. Thompson, Chicago, Iodine in the Thyroid Gland.
C. Alexander Hellwig, Wichita, Kan., Morphogeographic and Experimental Studies on the Etiology of Goiter.
Harold L. Foss, Danville, Pa., When Is a Goiter Toxic?
John deJ. Pemberton and John M. McCaughan, Rochester, Minn., Hemiaplasia of the Thyroid Gland.
William Weston, Columbia, S. C., Studies in the Prevention of Goiter.
Charles H. Mayo, Rochester, Minn., Thyroid Deficiency: A Commonly Unrecognized Disorder.
Richard B. Cattell, Boston, Diseases of the Thyroid in Children.
Willard Bartlett, St. Louis, Rehabilitation of the Toxic Patient Viewed in a New Light.
Frederick A. Coller and Walter G. Maddock, Ann Arbor, Mich., Water Balance of Patients with Hyperthyroidism.
Arthur E. Hertzler, Halstead, Kan., Indications and Technic for Complete Thyroidectomies.
Charles H. Frazier, Philadelphia, Carbohydrate Metabolism in Its Relation to Hyperthyroidism: A Continuation Study.
Benjamin Markowitz, Bloomington, Ill., Life Cycle of the Thyroid Cell and Its Relation to Goiter.
Martin Nordland, Minneapolis, Advantages and Technic of Preliminary Hemostasis in Thyroidectomy.
James A. Lehman, Philadelphia, Hyperthyroidism Complicating Pregnancy.
Shelby W. Wishart, Evansville, Ind., Use of Digitalis Preparations in Thyrotoxicosis.
Andre Crotti, Columbus, Ohio, Thyrotoxic Goiter Problem and the Autonomic.
Henry H. Searls and Wallace I. Terry, San Francisco, Further Observations on Parathyroid Protection.

Other speakers on the program whose subjects have not been announced include Drs. George W. Crile, Cleveland; Donald Guthrie, Sayre, Pa.; Emil Goetsch, Brooklyn; James A. Hill, Houston, Texas; Samuel J. Waterworth, Clearfield, Pa., and Ambrose G. McGhie, Hamilton, Ont. In addition, there will be clinics.

Government Services

The Lowest Army Venereal Disease Record

The lowest admission rate for venereal disease in the history of the U. S. Army, 45.6 per thousand, is announced in the recent annual report of the Surgeon General which covers the general activities of the medical department for the fiscal year ended June 30, 1932. The admission rate for venereal disease in the army in 1901 was 150. The surgeon general points out that automobiles again caused the greatest mortality, accounting for ninety-two deaths, an increase of 28 per cent over 1930 and 100 per cent over 1929. In a large number of the cases, faulty driving was said to be clearly the cause of the fatality. During the calendar year 1931, there were 623 deaths among officers and enlisted men of the army as compared with 533 in 1930, giving the highest death rate since 1920; 334 of these deaths were from disease and 289 from external causes. There were increases over the preceding year of fifteen deaths from tuberculosis; twenty-two from cardiovascular-renal disease; eight from suicides and homicides; twenty-five from railroad and automobile accidents; seventeen from airplane accidents and seventeen from pneumonia. Only one death due to malaria occurred among 868 cases in the entire army. A survey of the leading causes of death during a twenty year period, excluding the four abnormal years 1917-1920 and ending with 1929, shows that suicide was the leading cause in sixteen of the twenty years and tuberculosis in the other four. The admission rate to sick report was 655 for all causes as compared with 608 per thousand men in 1930. Respiratory diseases are of increasing importance as causes of admission. Fifty-three officers and 1,985 enlisted men were discharged from the service for disability. Diseases of the nervous system are the most important causes of discharge. During 1931, there were 1,608,143 days lost from duty on account of sickness and injury, an increase of 61,357 days over 1930. Of this time lost, 1,299,606 days were lost on account of diseases and 308,537 on account of injuries produced by external causes. Gonorrhea was the leading cause of loss of time with 43.1 days per case, and 3,566 cases. Notwithstanding the low rate, venereal diseases were responsible for 6,171 admissions and 245,007 days lost. Tuberculosis with only 316 cases was second, with an average of 327.7 days per case. There were thirty-nine deaths due to airplanes and balloons during the year, an increase of 17 over 1930, but twelve less than in 1929. The daily average number of patients hospitalized was 6,783. In addition, there were 989,708 outpatients treated with an average of a little less than two treatments per patient. There were 286,770 physical examinations made and 197,839 vaccinations administered. Of the 6,783 hospital patients, 58.3 per cent were army personnel and 28.8 per cent were beneficiaries of the Veterans' Administration. The cost per patient day in the general hospitals of the United States, including the station hospital, Fort Sam Houston, Texas, and exclusive of new construction, was $5.03, a decrease of 4 cents a day. Nine new station hospitals were opened during the year and one, Fort Eustis, Va., was closed. At present there are not enough medical officers to carry on the professional work of the army as desired. The enlisted strength of the medical department on June 30, 1932, was 6,528. The authorized allowance of 5 per cent of the total strength of the regular army in time of peace is entirely too small and should be increased to 7 per cent. At the present time there is practically no personnel for assignment to medical department field units, and posts and stations throughout the army have detachments that are inadequate. The increase in the total strength of the reserve corps was the largest since 1927. In the reserve officers' training corps units, the total enrolment during the year was 4,566, of which number 3,276 are in the medical units. Surgeon General Patterson emphasizes that the efficiency of the medical department is hampered by inadequate personnel. A comprehensive bill, representing the principal requirements of the medical department, will be recommended for introduction to Congress as soon as the national finances indicate that it may be given the consideration it merits.

Foreign Letters

LONDON

(From Our Regular Correspondent)

April 1, 1933.

The Size of the Modern Englishman

In the *Journal of the Royal Army Medical Corps*, Major M. J. Williamson has used the records of the gymnasium of the Royal Military Academy, which give the physical measurements of all the cadets who have passed through since 1865, to show any change in the last sixty years. For purposes of comparison, the records of sixty cadets were taken from the roll of 1870 and onward as they came. At the time of leaving, their average age was just under 20, their average height 5 feet 8 1/10 inches (173 cm.), and their average weight 10 stone 2½ pounds (142½ pounds, or 64.6 Kg.). On the other hand, the average height and weight of the entries in August, 1932, was 5 feet 10 inches (177.8 cm.) and 10 stone 8½ pounds (148½ pounds, or 67.3 Kg.), although the average age was lower—only 18½ years. These cadets are boys of the better classes who mostly come from "the public schools." Major Williamson has no doubt that the physical standard of these boys is definitely on the up grade. He attributes this to better feeding at the public schools—the additional supply of vitamins and the more or less correct amount of calories. Confirmatory evidence is the fact that the weights of the 1920-1922 cadets were below those of ten years before and ten years afterward. The drop is explained by the bad feeding in the later years of the war.

The Burden on Industry of Workmen's Compensation

The extraordinarily wide manner in which workmen's compensation for accident is awarded has been shown recently (THE JOURNAL, March 4, p. 673). In a letter to the *Times*, Sir John Collie, whose experience with the medical aspect of compensation cases is unique in this country, points out that the official estimate of the cost of compensation is $60,000,000 a year and that this probably errs on the conservative side. The secretary of the Industrial Welfare Committee holds that this figure should be trebled when the incidental and indirect losses are taken into account. The workmen's compensation act was intended to be comprehensive, limited only by the words "arising out of and in the course of the employment." But Sir John thinks that to make one man liable for the crass stupidity, gross carelessness or flagrant breach of orders by another did not come within such comprehension at the time. Yet such has been the legal interpretation of the act. Moreover, the psychologic effect on the workman of the certainty of compensation under all conditions is great. It leads to the taking of unnecessary risks which would not be done if he had to suffer for his own folly or disobedience of rules, as he has to apart from his work. There are grounds for thinking that quite a number of slight but compensatable accidents occur when trade depression is looming. Sir John therefore asks for a recasting of the act so as to bring it into conformity with the original intentions when it was passed. However just and desirable this may be, not in the interests of employers, who must pass on all costs to the price of their products, but in the interests of overburdened British industry, it does not seem likely that anything will be done, as all political parties are too afraid of the labor vote to do anything that can be so easily represented as hostile to the working man.

A Rubber Esophagus

Mr. Arthur Edmunds, lecturer on surgery at the Westminster Hospital, has reported in the *British Journal of Surgery* a remarkable case in which he substituted a rubber tube for a large part of the esophagus, with almost complete restoration of function. The patient was a woman, aged 40, from whom he removed the larynx, part of the pharynx, the cervical esophagus, and a considerable part of the thoracic esophagus for squamous cell carcinoma. The operation necessitated a permanent tracheotomy and a gastrotomy. By establishing a pharyngeal sinus in the neck just below the hyoid bone, Mr. Evans was able to introduce the short end of a wide rubber empyema tube into the upper pharynx. This tube was made secure in the neck by tapes passing through the holes in the flanges and was connected by a long rubber tube with the gastrostomy opening, thus producing an external rubber esophagus. The device functioned quite well and no secondary growths followed. Now, twenty-three years after the operation, the patient is alive and well and able to enjoy life. She complains only that, if she catches a cold, the coughing upsets her and produces some chafing at the entrance of the tube into the stomach. The tubes are taken out regularly and boiled, and there is no unpleasantness from decomposing food. She can wear a dress that entirely conceals her condition from the world. She has, of course, lost her voice, but she has cultivated a whisper which is sufficient for social intercourse. She is able to take and masticate ordinary food, both solid and liquid, and to swallow it through the rubber esophagus.

Gerson's Salt-Free Diet Not Satisfactory

Since 1924 the treatment of tuberculosis by a salt-free diet has been advocated in Germany. Gerson propounded the theory that, in tuberculosis and some other diseases, sodium chloride is retained in the body and the metabolism of acids and bases is deranged. Like a good many German practices apparently highly scientific, this appears to be only pseudoscientific. The British ministry of health considered that the dietetic treatment of tuberculosis should be investigated and dispatched Dr. E. H. H. Pask, medical superintendent of the High Carley Sanatorium, to Gerson's clinic in Cassel and to Hermannsdorfer's clinics in Berlin. Dr. Pask found no evidence that even if the diet should be completely adopted there would be an appreciable improvement in the results of a sanatorium treatment. A special kitchen is necessary, the diets cost 30 per cent more than ordinary sanatorium diets, and they are too unpleasant for English patients.

A Trap for Tsetse Flies

After mosquitoes, the tsetse flies are the greatest menace to the health of tropical Africa. Some twenty species are the carriers of the trypanosomes of trypanosomiasis in man and of nagana in cattle and other domestic animals. At a meeting of the Zoological Society, Mr. R. W. Harris, a medical student, showed a film of his father's work in dealing with the fly, including the tsetse trap invented by him. As the flies are attracted by the sight of large living animals, Mr. Harris treated the hides of horses and cattle with fly-poison. But a number of the living baits died from absorption of the poison. Mr. Harris then replaced the horse or ox by a canvas framework of similar shape suspended from a tree on the shady edge of a thicket haunted by the flies. He noticed that on alighting on any part of the body of a living horse or ox, the flies crawled to the abdomen, where the skin was easier to pierce. He therefore left an open slit along the bottom of the framework, and on the middle of the upper surface he made a window to which was affixed a gauze fly-trap. The device worked. Vast quantities were caught. In the discussion Dr. Bevan, director of veterinary research in Southern Rhodesia, pointed out that the trap had been employed only for one species of tsetse and that as different species had different habits it had yet to be proved that it had a wide application. Mr. Nash, who had been engaged on research in Tanganyika, described a trap for the pupae of tsetse flies—

logs arranged so as to tempt the females to deposit their eggs. Every few weeks the logs were rolled so as to expose the pupae to the sun, which soon killed them.

PARIS

(From Our Regular Correspondent)

March 15, 1933.

The Paris Institute of Puericulture

The creation in France of scientific institutes of puericulture is of comparatively recent date. At first, these were merely consultation centers in the obstetric department, where nurslings were regularly weighed; advice was given to nursing mothers, and bottles of sterilized milk were distributed. The initiative in this field was taken by Professor Budin of Paris and by Dr. Dufour of Fécamp. These consultation centers, scattered all over France, have rendered important service in the crusade against child mortality, which had been high in France. Dr. Variot, who had devoted himself passionately to this work, was unwilling to abandon it when he reached the age of retirement and was supposed to give up his hospital department. He accordingly secured from the city of Paris financial aid for the creation of a special institute of puericulture, to be independent of obstetric hospital service. On his death, in 1919, a new institute was created with the aid, in part, of funds received from the American Red Cross, and was located temporarily in the barracks. The institute became attached to the Faculté de médecine as an annex and was opened to students. The site soon became too small. A large building has now been erected in the west end of Paris, on an area that became available through the demolition of old forts. The management of the new institute has been entrusted to Professor Pinard, who is already in retirement but who is active in spite of his advanced age (90). For years he was a Paris deputy in parliament and made contributions toward the improvement of legislation pertaining to children. The new institute was recently opened with official ceremonies, at which the president of the republic was present. The institute has three principal sections. In the center is the school proper, which, with the administration department and the quarters for 150 pupil nurses, contains all the rooms required for theoretical instruction. The laboratories, in particular, have the most modern equipment, thanks to the generosity of Madame Raba Deutsch. In the left wing are all the services of the hygienic and prophylactic dispensaries designed for the mother, the nursling and the child of school age: general services, various vaccinations and notably against tuberculosis, prophylaxis of congenital syphilis, control of hygiene of the eyes, nose, throat, ears and teeth, and physical education. In the right wing are the hospital services, where mothers who have nursing difficulties or weakly infants receive attention. The school trains physicians who are working for the university diploma in puericulture, and nurses who are candidates for the diploma of "visiting nurse," and particularly for the state diploma or the university diploma of visiteuse d'hygiène maternelle et infantile, bestowed by the Faculté de médecine.

Treatment for Vomiting of Pregnancy

Numerous articles are appearing in France on vomiting of pregnancy, to which widely different causes have been attributed. Some authors, Hinglais among the number, incriminate a toxic substance that is said to be secreted by the syncytial tissue of the placental villi; others seek the cause in an alteration of the hepatic function. Dr. Bec of Avignon assumes that the blood of the mother contains defense proteins that neutralize the effects of the toxic proteins coming from the fetal blood and the placenta. These are diastases, whereby the Abderhalden reaction is exemplified. The blood of pregnant women contains, moreover, a large number of abnormal substances; there is an excess of cholesterol, a substance considered antitoxic and antihemolytic. Mr. Bec therefore conceived the idea of employing, in women affected with grave vomiting, the blood serum of mares during gestation. This blood serum, collected in ampules for injection and sterilized, was administered, in these cases, in doses of from 10 to 30 cc. a day. The effects were remarkable. The vomiting, the aversion to food and the ptyalism are checked—sometimes within a few hours, but within two or three days, at the longest, if the injections are repeated. Generally, after an adequate period of treatment, the effects become permanent, and the pregnancy continues without further mishap. Some maternities are now keeping a supply of this serum in stock.

The Protection of Foodstuffs

Various protests have been made against the contamination of foodstuffs exposed for sale in front of stores. These shops are often open early. In Paris and other large cities, the cleaning of streets is accomplished by sprinkling, which keeps down the dust. In the small towns, however, the streets are still swept with dry brooms, which raise dust. The sidewalks everywhere are likewise swept, the police regulations requiring each house owner to keep the sidewalk clean in front of his property. At present, and much more than formerly, the sidewalks are covered with all sorts of filth. The Academy of Medicine, having been requested by the municipal council of Paris to express its opinion on this subject, appointed a commission to study the question. The commission announced its conclusions through Dr. Brouardel, which were adopted unanimously. It recommended, of course, that foodstuffs be protected against external contamination, and suggested various methods. Bread and cakes should be protected by transparent coverings. Meat and fish should never be exposed outside of shops. The protection of fruit is more difficult, as people are inclined to handle it before making a selection, and fruit is frequently sold from carts that pass through the streets. The instructions recommended to the public that all fruit be washed thoroughly under the faucet, at least an hour before being served on the table, in order that it may have time to dry without having to be dried with a towel. It is likewise recommended that the surface of pieces of meat be exposed to a flame for a few seconds as soon as they are brought into the kitchen, with a view to sterilizing them superficially until they can be cooked.

Cobra Venom in the Treatment of Cancer

Mr. Laignel-Lavastine and Mr. Korossios have experimented with cobra venom in the algias of cancer patients. They used doses of 0.001 mg., which is relatively high. Cancer patients who required daily injections of heavy doses of morphine observed that their pains ceased with the first injections of venom, so that the regular use of morphine could be discontinued. The injection needed to be repeated only every eight or ten days. A few days later, at a session of the Academy of Medicine, Professor Gosset gave an account of the research carried out on the same subject in the laboratory of his surgical service in the Hôpital de la Salpêtrière. They also observed a relief from pains in inoperable neoplasms, and likewise an improvement in the neoplasms themselves. In some instances, distant metastases disappeared. The patient increased in weight. One cannot speak of cancer being cured, but an unquestionably salutary effect could be noted. These researches are to be continued.

Dedication of Institute of Serology

Last year, at the commemoration of the hundredth anniversary of the birth of Prof. Alfred Fournier, it was decided to create an institute of serology that should bear his name. This institute has been completed and was recently dedicated

by ceremonies, to which the ministry of public health and the Ligue d'hygiène sociale sent representatives. A paper on the present state of serologic diagnosis and treatment of syphilis was presented by Professor Levaditi, of the Institut Pasteur, and another by Dr. Sicard of Plouzolles, director of the institute. There followed an inspection of the laboratories, which are equipped with the latest improvements. Special provision is made for research on the effects of physical agents on serums. Mr. Levaditi will be in charge of one of the laboratories.

PRAGUE

(From Our Regular Correspondent)

Feb. 27, 1933.

The Public Health Budget

The state budget for 1933, including the allotment for the ministry of health, was recently passed by the chamber of deputies. The whole state budget, which amounted in 1932 to about 9 billion 300 million crowns, was cut to 8 billion 6 million crowns, a reduction of about 7.8 per cent. The budget for the ministry of health, which amounted in 1932 to about 150 million crowns, was cut to 146 million, a reduction of about 2.5 per cent. (The rate of exchange for the crown is about 3 cents.) The minister of health, Dr. Frank Spina, in forwarding his budget stressed the importance of maintaining public health work on a high level of efficiency. The chief concern of the public health administration is the public health dispensaries, which have developed since the war into an important agency for protecting the masses from social diseases. These dispensaries are chiefly administered by voluntary organizations, which are in a difficult financial situation at present. Public authorities had to step in to assure the continuation of their activities. It would be unwise to reduce these stations when a large part of the population is unemployed. A special institution for the treatment of tuberculosis of the skin is being planned and financial means have been secured for constructing a special treatment center in Prague. Intense efforts will be directed against diphtheria, which was epidemic last year in Czechoslovakia far more than in any other year since the war. Free vaccine will be furnished for indigent children. The Calmette vaccine, the use of which has been reduced since the Lübeck incident, also will be furnished free to indigent children. In spite of the depression, more than 400 water supplies are under construction all over the country. The latest project calls for the erection of a new hospital for the state medical schools of Prague which is to commence this year and to be completed in eighteen years. An intensification of public health work is planned for territories where the need is greatest, especially the eastern half of the country, where the situation in rural areas is bad. Thirty-seven public health and treatment centers are being maintained there from public funds. If the financial situation does not necessitate further reductions, the public health can be considered sufficiently safeguarded at least for 1933.

The Recent Influenza Epidemic

The Association of Czech Physicians in Prague devoted a meeting to a discussion of the influenza epidemic which occurred in Bohemia last December and January. The discussion centered around the etiology of influenza, the exact diagnosis of which is impossible. The influenza bacillus was found only in rare cases at the beginning of the epidemic; on the other hand, Streptococcus haemolyticus was found quite frequently. The theory that influenza is always present finds its chief difficulty in the fact that the picture of the disease changes from year to year. The peculiarity of this epidemic was that it tended to two or three relapses and the later ones were usually more serious than the first attack. In many cases there was an interval as long as fourteen days between the two attacks. Frequently the disease attacked at the same time a whole family, which it had not been in the habit of doing in Czechoslovakia since 1920. Often serious changes in the lungs could not be found by percussion or auscultation but could be easily seen in a roentgenogram. The disease was regularly accompanied by leukocytosis. The most frequent complications affected the ear and the throat, leading sometimes to acute edema. It was curious that the epidemic appeared weeks earlier among children, in whom it did not take an especially unfavorable course. The outbreak was accompanied by rather unusual weather, with a high pressure and considerable cold and fog. The epidemic was about as intense as that of 1920.

State Recommends Types of Clothing

The state institute of public hygiene of Prague is developing a novel line of activity. In its laboratory for the study of hygienic clothing it endeavors to work out types of clothes which will be practical and at the same time answer all the requirements of modern hygiene. Clothing is an important item in the family budget. It would be futile to attempt to influence that part of human clothing which is subjected to the fluctuations of fashion, so the work of the laboratory has been concentrated on the study of types of working clothes. The laboratory proposed a type of clothing for certain activities and presented the proposal to a group composed of hygienists, economists, and experts in textile industry and art. When this body approved the type it was recommended to the public for general trial. Such types of clothes have been worked out for peasant women, gardeners, office workers and the school children. Recently an exhibit was presented. By educational propaganda the laboratory attempts to introduce for general use the types that have been worked out. The laboratory also makes scientific studies of materials used. The types recommended are slowly coming into general use.

BERLIN

(From Our Regular Correspondent)

April 3, 1933.

Measures to Prevent Overcrowding of Universities

In view of the large number of pupils graduating from the secondary schools, the crowded universities, and the depressed state of the academic labor market, the administrations of public instruction in all German *länder*, beginning with the Easter recess, 1933, will apply the following regulations in recommending graduates of secondary schools for admission to higher schools of learning: An examining board in every secondary school will consider carefully not only the scholastic records of each individual candidate but also his human qualities, mental aptitudes, and his predilections and general performances, and on this basis decide whether or not to recommend a pupil for advanced studies. The school administration will acquaint the parents of the pupils who cannot be recommended with the decision of the examining board. Likewise, on request, university authorities will be informed of the decision of the secondary school in any case, but the information will not be given out promiscuously. Any pupil who, contrary to the advice of the secondary school from which he was graduated, persists in taking up advanced studies, cannot count on receiving any special favors in connection with his studies. Pupils who enter universities without a recommendation will be on probation for the first three semesters. Such pupils must demonstrate their suitability, and the results of any reexamination will be considered in all further tests and in granting applications for admission to the "seminar" and other drill work. The federal commissioner for the Prussian ministry of science, art and public education has issued the following statement: The Prussian administration of public instruction has given its approval to the agreement

adopted by the several *länder* whereby the overcrowding of our universities and schools of higher learning is to be checked. While graduates of secondary schools who are not especially suited for advanced study are not to be absolutely excluded from attendance at a university, the attention of such pupils must be earnestly called to the probable unhappy outcome of their choice of an academic profession in the face of the opposing advice of the authorities of the secondary school from which they were graduated.

The Vitamin C Content of Milk

An important duty of producers of various brands of powdered and condensed milk is to see to it that the milk shall contain the required amount of vitamin C, the antiscorbutic vitamin. A deficiency of vitamin C, which often occurs during the winter when cattle are confined to their stalls, may be a menace to the health of children, even though scurvy in its clinical form may not develop. Now that the nature of vitamin C is known in a general way (doubtless a highly reducing acid, probably belonging to the sugar group), research on the quality of milk has been greatly facilitated. A simple color test has been worked out that enables the analyst to estimate the ingredients of milk. Schlemmer, Bleyer and Cahnmann, who discuss the significance of this test in the *Biochemische Zeitschrift*, bring out that if cows receive the correct food even winter milk will contain sufficient vitamins. Their research confirms that milk exposed to the open air and to a higher temperature suffers a loss of vitamins. Bringing milk to a boil causes an almost negligible impairment; pasteurization causes more impairment. In preparing milk for use it was found that, in addition to the injurious effects of exposure to air, the kind of metal of which the apparatus is composed is important. The much used copper apparatus injures in a pronounced manner the vitamin content; tin is less injurious. Nickel, chromium and aluminum exert practically no damaging effects.

Widespread Charlatanry

Attention is being called again and again to the unendurable situation that has arisen as a result of widespread charlatanry and the marketing of fraudulent medicinal remedies. It has afforded great satisfaction that the Prussian minister of the interior, March 17, issued the following proclamation: "I again call attention to the need of the strictest observance of the joint regulation of the Prussian ministry of commerce and industry and the ministry of public welfare. In the interest of our health seeking compatriots, who are often bereft of funds, it cannot be permitted that fraudulent medicinal remedies shall continue to be sold on the streets and through house-to-house canvassing, at exorbitant prices. I demand, therefore, that this harmful practice be most rigorously suppressed."

Professor Meyer's Eightieth Birthday

The recognized leader among German pharmacists, Prof. Hans Horst Meyer of Vienna, celebrated his eightieth birthday, March 17. At the age of 29, he held the chair of pharmacology at the University of Dorpat, Estonia. From Dorpat he was called to Marburg; in 1904 he was given the chair of pharmacology in Vienna, and, refusing a call to Berlin, he held this position until he reached the age of enforced retirement. He and the pharmacologist Gottlieb of Heidelberg published "Experimentelle Pharmakologie als Grundlage der Arzneibehandlung," which, on its appearance in 1910, was the only work of its kind in existence and hence passed through several editions within a short time. On his seventieth birthday, the Vienna Academy of Sciences established the Hans Horst Meyer prize, which is bestowed every five years for the best research in the German language in the field of experimental medicine. The influence that Meyer's teachings have had on research and on practical therapy has been great.

International Commission on Circulatory Disturbances

As an outgrowth of the Kongress der Deutschen Gesellschaft für Kreislaufforschung, held in Würzburg, an international commission for research on, and the combating of, disturbances of circulation was created. England and the United States, Bulgaria, Rumania, Denmark, Sweden, Norway, Belgium, Czechoslovakia, Italy, Austria and Switzerland, in some of which countries corresponding organizations already exist, are participating in the movement. The first session, under the sponsorship of the American committee, will be held in June, 1934, in the Kerckhoff-Herzforschungsinstitut in Bad Nauheim.

ITALY

(From Our Regular Correspondent)

Feb. 28, 1933.

Congress of Orthopedics

The twenty-third Congresso nazionale di ortopedia was held at Bologna, under the chairmanship of Professor Putti. A number of foreign surgeons were in attendance. In his address, Professor Putti brought out that the work of the congress would be based on observations in more than 4,000 cases of congenital dislocation of the hip, all of which had been reexamined radiologically at least three years after operation. He pointed out that the incidence of this abnormality amounts to about 2 per thousand of population. The chief speaker was Professor Annovazzi of Milan, who based his conclusions on 1,610 cases. In the children treated under 2 years of age, the percentage of good results was 82 per cent; in children under 5 and more than 2 years of age, 66 per cent, while in children more than 5 years old the percentage of favorable results diminished gradually. These statistics show the need of resorting to the operation as early as possible.

Professor Spitzy of Vienna described a method of reconstructing the cotyloid cavity by inserting above the head of the femur (without opening the capsule) a strip of bone taken from the tibia. Professor Putti reported the results secured in the Istituto ortopedico Rizzoli in Bologna in 3,216 cases treated from 1899 to 1927. He brought out that the greater part of the complications arising in the treatment of the luxation must be attributed to the traumatic factor, and that in order to reduce the trauma to a minimum it is necessary to intervene early, after a diagnosis made a few days after the birth of the child.

The next congress will be held at Palermo. Chief topics on the program will be: (1) Criteria and Modern Methods in the Treatment of Fractures, and (2) Arthrodesis in Osteo-Articular Tuberculosis.

Apicolysis in Treatment of Tuberculosis

The Latium chapter of the Federazione nazionale per la lotta contro la tubercolosi met in Rome under the chairmanship of Prof. Eugenio Morelli. Di Fonzo spoke on the use of a small rubber balloon in the application of apicolysis. The stimulation for this research came from a suggestion of Professor Morelli, who, in 1931, recommended the experimental application of apicolysis by introducing into the extrapleural space a small rubber balloon, to be filled with air from the outside. The intervention is carried out anteriorly, a small portion of the second rib being resected. Over the balloon, filled with filtered air, the layers of muscles are spread. The stem of the balloon is retained under the skin during the first week, lest the space it occupies should serve as a path to possible infections. The postoperative course of patients treated by this method was good.

Prof. Omodei Zorini explained the clinical indications for simple apicolysis and apicolysis with plugging. He called attention to the disadvantages of plugging with paraffin; among

others, the possibility that the foreign body introduced between the costal walls and the fibrous cavity, not being sufficiently elastic, may stimulate the morbid process. Apicolysis is indicated also in case of large isolated cavities in the apex and in the subclavicular region. In subjects with fibrous tuberculosis of the apex and with cavities not more than 2 cm. in diameter, the speaker stated that good results can be secured by effecting a total extrapleural detachment of the apex and closing the wound.

Professor Ascoli described the technic of simple apicolysis as proposed by Tuffier. The prevailing conception of the method is to collapse the cavity and, more generally, the diseased areas of the lung. This treatment is useful only in the types that have shown a tendency to retraction. By ample resection of the second rib anteriorly, all the maneuvers of pleuroparietal detachment can be performed under direct vision through an opening that permits the introduction into the thorax of the hand of the operator. It is thus possible to liberate the pleural dome from the ligaments that support it and effect a complete apicolysis.

Monaldi summarized the first ten cases in which apicolysis was done in accordance with the technic described by Ascoli. The immediate postoperative course was characterized by a moderate effusion (which was absorbed within fifteen days) into the cavity formed as a result of the operation. There was a febrile temperature for from three to eight days, and increased expectoration. There has never been any diffusion of the process. The therapeutic results have not been so good in patients in whom the area of the lung that surrounded the cavities was ample and not well circumscribed. Favorable results were, however, observed in a group of subjects in whom the cavity or the cavities were surrounded by a condensed, well circumscribed area.

Meeting of Radiologists

The fifteenth session of the radiologists of the Gruppo centro-meridionale Saldo-Siculo was held in Palermo. Professor Castronuovo of Messina, speaking on radiotherapy in diabetes insipidus, pointed out that pituitary preparations effect an improvement of the polyuria, but roentgen therapy applied to the hypophysis brings about a notable improvement in the general condition of the patient. Dr. Rizzo of Palermo treated four cases of malignant tumors of the tonsil with radiotherapy and effected two cures, one of which dates back six years. Professor Zanela of Palermo obtained good results (some of the cases dating back five years or more) with roentgen therapy in cancer of the uterus and attained 80 per cent of cures in cases treated in the beginning stage. He emphasized the need of administering the maximal dose.

Professor D'Istria of Naples reported some bone lesions due to birth injuries and emphasized the necessity of roentgenograms taken after a certain interval, in order to give periosteal hematomas a chance to develop, as they may be the only visible radiologic sign of bone lesions due to calcification. Professor Canavò reported a series of cases of bronchospirochetosis in which the radiologic pictures resemble those of chronic bronchitis. Professor Busi of Rome described a case of ileocecal fistula following an operation for gangrenous appendicitis, in which the radiographic examination revealed the presence of a portion of the appendix, which was the cause of the suppuration. Dr. Vita spoke on duodenal ulcers, which, he said, originated in the serous membrane and are frequently associated with cholecystitis and appendicitis.

Three communications, presented by the school of radiology in Naples, concerned the use of a 25 per cent solution of thorium dioxide. Professor Tandoia spoke of certain structural changes that he had found in the liver in certain persons. Vaiano considered the possibility of making the placenta radiologically visible in vivo in animals with doses that harm neither the fetus nor the maternal organism.

Marriages

COLVIN BURR CHILDS, Surg., Lieut. Commander, U. S. Navy, to Miss Claretta Reese of Lake Forest, Ill., March 18.

ERNEST HUTCHINSON MENGES, Nantucket, Mass., to Miss Susan Julia Mayer Van Kleeck of New York, March 20.

EUGENE SCOTT BROWN, Tioga, W. Va., to Miss Margaret Louise Huddleston, at Summersville, February 25.

HYMEN LEON COHEN, New Orleans, to Miss Pauline Weil Herzfeld of West Point, Ga., March 22.

MORRIS J. BROOKS to Miss Bessie Finkelstein, both of Brooklyn, April 9.

Deaths

Charles Oliver Probst ✠ Columbus, Ohio; Miami Medical College, Cincinnati, 1882; member of the Public Health Council, State Department of Health; for twenty-five years secretary of the state board of health; member of the American Climatological and Clinical Association and the National Association for the Study and Prevention of Tuberculosis; past president of the American Public Health Association and the Ohio Society for the Prevention of Tuberculosis; past president and secretary of the Conference of State and Provincial Boards of Health; for ten years professor of hygiene, Starling Medical College; medical superintendent of the Franklin County Sanatorium; aged 75; died, April 2, of pneumonia.

Edward Antoine Rich ✠ Tacoma, Wash.; Jefferson Medical College of Philadelphia, 1901; fellow of the American College of Surgeons; veteran of the Spanish-American and World wars; aged 56; orthopedic surgeon to the Pierce County Hospital, St. Joseph's Hospital, Northern Pacific Beneficial Association Hospital and the Tacoma General Hospital, where he died, March 22, of burns and shock suffered when gasoline aboard his yacht exploded.

Joseph Stanley Lichtenberg ✠ Kansas City, Mo.; University Medical College of Kansas City, 1896; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; ophthalmologist to St. Joseph's and Kansas City General hospitals and the Alfred Benjamin Dispensary; aged 63; died, April 2, in the Menorah Hospital, of gas bacillus septicemia following a prostatectomy.

William James Arm Derome, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1895; formerly associate professor of clinical surgery, University of Montreal Faculty of Medicine; fellow of the American College of Surgeons; surgeon to the Hotel Dieu de St. Joseph and Montreal Chinese Hospital; aged 64; died, March 7.

Wilborn Arthur Upchurch, Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1903; member of the Medical Association of Georgia; fellow of the American College of Surgeons; served during the World War; chief urologist to the Grady, Atlanta, Georgia Baptist, and Crawford W. Long Memorial hospitals; aged 49; died, March 27, of wounds received when shot by bandits.

Irving Dewey Williams ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1903; member of the Medical Society of New Jersey; medical director and superintendent of the Central Park West and Towns Hospitals; aged 60; died, April 7, in the Battle Creek (Mich.) Sanitarium, of Hodgkin's disease.

George Slocum ✠ Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1889; professor of ophthalmology at his alma mater; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; aged 67; died suddenly, March 24, of heart disease.

Garrette Van Sweringen ✠ Fort Wayne, Ind.; Fort Wayne College of Medicine, 1903; Jefferson Medical College of Philadelphia, 1905; past president and secretary of the Allen County Medical Society; on the staff of the Fort Wayne Lutheran Hospital; aged 50; died, March 29, of heart disease.

William E. Shackleton ✠ Cleveland; Cleveland College of Physicians and Surgeons, Medical Department of the University of Wooster, 1895; member of the American Academy of Ophthalmology and Oto-Laryngology; on the staff of St. Luke's Hospital; aged 63; died, March 27, of heart disease.

Adam Tyree Finch ✠ Chase City, Va.; University of Virginia Department of Medicine, Charlottesville, 1896; secretary and past president of the Mecklenburg County Medical Society; president of the county board of education; aged 60; died, February 22, of coronary thrombosis.

William Hayes Irwin ✠ Oakland, Calif.; Cooper Medical College, San Francisco, 1904; fellow of the American College of Surgeons; on the staffs of the Alameda County Emergency Hospital and the Providence Hospital; aged 56; died, March 13, of cerebral hemorrhage and hypertension.

Frederick William Mayer, Indianapolis; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; member of the Indiana State Medical Association; county health officer; aged 49; died, March 29, in St. Vincent's Hospital, of multiple myeloma.

Charles A. Cramton ✠ St. Johnsbury, Vt.; University of Vermont College of Medicine, Burlington, 1893; fellow of the American College of Surgeons; oculist and laryngologist to St. Johnsbury and Brightlook hospitals; aged 61; died suddenly, March 21.

James Earle Dull ✠ Somerset, Pa.; University of Maryland School of Medicine, Baltimore, 1914; past president of the Somerset County Medical Society; served during the World War; aged 43; died, March 23, of acute nephritis.

Foster H. Bussey, Louisville, Ky.; Kentucky School of Medicine, Louisville, 1907; served during the World War; aged 53; died, March 26, in St. Anthony's Hospital, of hemorrhage of the stomach, cirrhosis of the liver and erysipelas.

John Austin Yates, Edmonton, Ky.; Kentucky School of Medicine, Louisville, 1890; also a druggist; member of the Kentucky State Medical Association; for many years county health officer; aged 72; died, March 26, of heart disease.

Donald Blair Fraser, Stratford, Ont., Canada; Faculty of Medicine of Trinity College, Toronto, 1874; formerly emeritus professor of histology, University of Western Ontario Medical School, London; aged 84; died, January 18.

Frank C. Curry, Milford, Ohio; Medical College of Ohio, Cincinnati, 1881; member of the Ohio State Medical Association; formerly health officer of Milford; aged 74; died, February 28, of angina pectoris and influenza.

Joseph B. Robinson, Hiattville, Kan.; College of Physicians and Surgeons, Keokuk, Iowa, 1878; Jefferson Medical College of Philadelphia, 1891; aged 74; died, January 6, at Fort Scott, of chronic myocarditis.

James Edward Coyle, San Antonio, Texas; Medical Department, University of Tennessee, Nashville, 1892; member of the State Medical Association of Texas; aged 71; died, March 20, of coronary occlusion.

Edgar L. Bossett Plant, Wheeling, W. Va.; Jefferson Medical College of Philadelphia, 1895; member of the West Virginia State Medical Association; aged 63; was found dead, March 23, of heart disease.

Edward R. M. Pennypacker, Newark, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1893; veteran of the Spanish-American and World wars; aged 66; died, March 24, of heart disease.

Harry Alfred Fulton, Havelock, Neb.; Medical Department of Omaha University, 1898; aged 64; died, February 24, at the Lincoln (Neb.) General Hospital, of diabetes mellitus and carbuncle of the neck.

Ben Edward Barham, Oak Ridge, La.; Medical Department of the Tulane University of Louisiana, New Orleans, 1912; aged 48; died, March 24, in a hospital at Monroe, of pulmonary tuberculosis.

Francois Lucien Sylvestre, Montreal, Que., Canada; University of Bishop College Faculty of Medicine, Montreal, 1892; on the staff of the Hospital Ste. Jeanne d'Arc; aged 65; died, January 23.

Frank Jackson Stewart ✠ Chicago; Harvey Medical College, Chicago, 1903; Chicago College of Medicine and Surgery, 1916; aged 57; died suddenly, March 31, in St. Luke's Hospital, of heart disease.

John Felix Wilson, Dalark, Ark.; Medical Department of Arkansas Industrial University, Little Rock, 1897; member of the Arkansas Medical Society; aged 61; died, January 15, of hypertension.

William Carter Heggie, Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1886; for many years on the staff of the Toronto Western Hospital; aged 67; died, February 20.

Charles William Matlock, Cedar Vale, Kan.; Loyola University School of Medicine, Chicago, 1917; aged 39; died, February 18, in St. Mary's Hospital, Winfield, of edema of the brain.

John Tees ✠ Reno, Nev.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1896; aged 62; died, February 3, of carcinoma of the right suprarenal with metastases.

John B. Ritchey, Pasadena, Calif.; Miami Medical College, Cincinnati, 1869; member of the Medical Society of the State of Pennsylvania; aged 92; died, February 13, of senility.

A. Ernest Bruce, Detroit; Detroit College of Medicine, 1905; aged 58; died, March 16, in the Highland Park (Mich.) General Hospital, of brain tumor and diabetes mellitus.

Millard F. Hamilton, Mannington, W. Va.; American Medical College, St. Louis, 1883; formerly member of the state legislature; aged 74; died, March 20, of heart disease.

William I. Linn, Prescott, Ariz.; Columbus Medical College, 1882; past president of the Yavapai County Medical Society; aged 76; died, February 17, of myocarditis.

Edwin M. Miller ✠ Los Gatos, Calif.; Ensworth Medical College, St. Joseph, 1897; aged 63; died, February 16, in the O'Connor Sanitarium, San Jose, of heart disease.

Donald Herbert Linard ✠ Cleveland; Jefferson Medical College of Philadelphia, 1926; aged 31; died, March 26, of pneumonia, following an operation on the throat.

William Herman Wiesjohn, Chicago; Chicago Medical School, 1927; member of the Illinois State Medical Society; aged 47; died, March 31, of acute myocarditis.

Harry O. Philp, Benton, Ill.; Missouri Medical College, St. Louis, 1893; member of the Illinois State Medical Society; aged 63; died, March 22, of lobar pneumonia.

George Peck Brady, Chicago; Chicago Homeopathic Medical College, 1890; aged 72; died, February 9, in the Chicago Home for Incurables, of cerebral hemorrhage.

Arthur Guy Ashton Fletcher, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1894; served during the World War; aged 63; died, in March.

Ella Pringle Brown, Oakland, Calif.; University of Oregon Medical School, Portland, 1896; aged 87; died, March 14, in a local hospital, of lymphatic leukemia.

John Wilson West ✠ Philadelphia; Jefferson Medical College of Philadelphia, 1886; aged 72; died, March 24, in St. Joseph's Hospital, of hypernephroma.

William Paul Coons, Chicago; National Medical University, Chicago, 1901; aged 60; was found dead, February 21, of cyanide poisoning, self-administered.

Barnett A. Rynerson, West Union, Ill.; University of Louisville (Ky.) School of Medicine, 1891; aged 81; died, March 6, of chronic myocarditis.

Julius Shenkin, Philadelphia; Medico-Chirurgical College of Philadelphia, 1899; aged 53; died, March 9, in the University Hospital, of brain abscess.

Davis Montgomery Thompson, Harrodsburg, Ky.; Bellevue Hospital Medical College, New York, 1869; aged 89; died, February 22, of influenza.

Franklin E. Haynes, Abilene, Texas; University of Louisville (Ky.) School of Medicine, 1894; aged 70; died, March 21, of cerebral hemorrhage.

Joseph O. Morrison, Fairfax, Minn.; Physio-Medical College of Indiana, Indianapolis, 1889; aged 68; died, March 24, of angina pectoris.

Onezime Edmond Belcourt, Lafleche, Sask., Canada; School of Medicine and Surgery, Montreal, Que., 1880; aged 80; died, January 31.

John Edwin Morton, Salt Lake City; Hahnemann Medical College, San Francisco, 1902; aged 59; died, March 5, of paralysis agitans.

James Lafferty, Hamilton, Ont., Canada; University of Toronto Faculty of Medicine, 1882; aged 73; died, January 20, of pneumonia.

Edward T. Juchhoff, Chicago; Chicago Hospital College of Medicine, 1918; aged 40; died, January 27, of chronic myocarditis.

Raymond d'Auteuil, Quebec, Que., Canada; Laval University Faculty of Medicine, Quebec, 1927; aged 28; died, January 10.

Joseph Elie Michaud, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, 1887; aged 69; died, Dec. 9, 1932.

Chauncey A. Mead, Everett, Wash.; Kentucky School of Medicine, Louisville, 1884; aged 71; died, January 19, of toxemia.

John Colbert McAfee ✠ Macon, Ga.; Baltimore Medical College, 1898; aged 59; died, March 27, of heart disease.

Bureau of Investigation

PHENOLPHTHALEIN AS A "PATENT MEDICINE"

The Public Health Menace of Self-Administered Candy Cathartics

In a bulletin issued by the Office of Information of the United States Department of Agriculture as part of its present service and released to the newspapers April 11, Dr. F. J. Cullen of the Federal Food and Drug Administration warns against the dangers to the public health in the widespread exploitation of phenolphthalein put up in the form of confections and sold to the public for self-administration. The warning has come none too soon. Physicians have for some time past awakened to the fact that phenolphthalein is by no means harmless and that its indiscriminate use carries with it a very real danger.

Phenolphthalein was introduced into medicine as a laxative about thirty years ago, following the observation that certain of the cheaper Hungarian wines to which it had been added took on an actively laxative effect. Phenolphthalein is an odorless and almost tasteless powder, very slightly soluble in water. It is practically insoluble in acids, and passes through the stomach unchanged. From the fact that it is nearly tasteless and is active in small doses, it is especially well adapted for the production of what have been called candy medicaments. Among its disadvantages is a degree of variability in action, small doses sometimes acting excessively, when at other times a larger dose will fail to act. It may cause, in addition to purgation, colic, rapid pulse, difficult breathing, and even collapse.

Hydrick as long ago as 1914 reported a case of albuminuria lasting from one to three days following the administration of phenolphthalein in doses of from one to two grains. Fuerbringer in 1917 reported a case of poisoning following the taking of about nine grains of phenolphthalein by a woman who developed cardiac weakness, a rapid, intermittent, irregular and thread-like pulse, with irregular respiration and dyspnea and some mental confusion. Later the patient developed a trace of albuminuria and an almost total anuria. Holz has reported observing severe gastro-intestinal disturbances, hematuria, chill and pain suggesting renal stone colic.

Abramowitz in 1918 was the first to report, what has since become a matter of common medical observation, a skin eruption following the administration of phenolphthalein. Wise and Abramowitz, in the *Archives of Dermatology and Syphilology* for March, 1922, reported a number of cases of skin eruption. Ayres in THE JOURNAL in 1921 reported two cases of phenolphthalein dermatitis. Corson and Sidlick in the same publication and the same year reported a case of urticaria from the habitual use of phenolphthalein. Rosenbloom, also in THE JOURNAL in 1922, reported a case of nasal herpes.

Wise, in THE JOURNAL of April 9, 1927, stated that one of the most common causes of recurring ulcers of the mouth undoubtedly lies in the ingestion of drugs and that phenolphthalein comes first in the production of such untoward effects. Ely reported in THE JOURNAL, Jan. 23, 1932, a case of a child of less than three years who had been given five "Analax Tablets" in thirty-six hours. The lips and eyelids became swollen and a bright red eruption broke out on the exposed parts.

Cleeves, in THE JOURNAL, Aug. 20, 1932, reported the case of a healthy ten-year-old boy who ate the contents of a box of "Ex-Lax Tablets" in mistake for candy, and died. The child's temperature rose to 106, an eruption of huge wheals appeared on the abdomen, legs and arms, hemiplegia developed, the child became delirious, and nine days after taking the Ex-Lax Tablets, died.

It is, of course, no argument against a drug to report cases of untoward effects or morbidity or fatality following its use where such use has been excessive. There may be no serious objection to a physician's prescribing for a child phenolphthalein in candy form, because the very conditions that surround the issuance and use of a prescription are such as to make it highly improbable that the dosage recommended will be exceeded. It is an entirely different thing, however, to put up an active drug in the enticing form of candy or chewing gum, sell it indiscriminately to the public for self-medication, and advertise it in newspapers and over the radio by the ballyhoo methods common to "patent medicine" exploiters.

It is a well-known fact that the public has a general idea that even products that are of an obviously medicinal character which are sold as "patent medicines"—that is, as package medicines for self-administration in the treatment of self-diagnosed conditions—are, broadly speaking, harmless. They have a feeling that the state—using the term "state" in its broadest sense—would not permit the indiscriminate sale to the public of drugs that were really dangerous. How far this is from the truth, every physician knows, but the fallacy persists.

The facts are, there is no legitimate excuse for putting up potent drugs in the enticing form of confections and selling them indiscriminately to the public.

Correspondence

LABORATORY EXAMINATIONS IN DIABETES AND IN GASTRIC DISORDERS

To the Editor:—In the editorial comment on serum amylase (THE JOURNAL, March 11) appears the following: "Chemical examination of the blood . . . has displaced the older chemical examination of the urine in several directions, such as for the study of the diabetic state." Such a statement is not in accord with the facts. When studying the diabetic state the physician is primarily concerned with the metabolism of carbohydrate and the ability of the patient to utilize the carbohydrate ingested. Blood sugar estimations are of occasional importance in determining the existence of the diabetic state; i. e., in differentiating true diabetes from nondiabetic glycosuria. Occasionally the renal threshold for dextrose is so high that glycosuria does not occur in the diabetic state, so that blood sugar determinations afford the best means of ascertaining the individual's carbohydrate metabolism. But after the diagnosis of diabetes has been established and the renal threshold value is determined to be at or about the normal level, the next step is to determine the patient's capacity for carbohydrate metabolism—to measure the intake and output of dextrose. At the same time the carbohydrate intake must be adjusted so that the patient, with or without the assistance of insulin, does not excrete dextrose. Blood sugar estimations do not, and can not, displace the all important urine examination during this lengthy and most important stage in the management of uncomplicated diabetes. When the diabetic state is accompanied by incomplete metabolism of fat, with or without coma, examination of the carbon dioxide combining power of the blood is of importance. But because of the equipment, time and technical skill required for such determinations it seems doubtful that they will supplant the simple, well known urinary tests for acetone and diacetic acid.

In the second sentence the statement is made that "abnormalities of gastric function can be investigated by withdrawal of the contents of the stomach." Such a statement would lead one to believe that gastric analysis is of considerable value in diagnosis or treatment of gastric disorders. Gastric hemorrhage, true achlorhydria, and sometimes advanced gastric malignancy are conditions which might be profitably investigated by means of gastric analysis. But the remaining vast majority of gastric disorders having to do with motility or secretion have yet to be proved to be helped, either diagnostically or therapeutically, by gastric analysis. In confirmation of this view are editorials in THE JOURNAL (Gastric Acidity, Sept. 24, 1932, p. 1087; Significance of Gastric Acidity, April 2, 1932, p. 1187; Unexplained Anacidities, Feb. 6, 1932, p. 485; Gastric Hyper-

acidity? June 27, 1931, p. 2199), to say nothing of the numerous pertinent articles in the recent literature.

Every day many gastric analyses and blood examinations are performed with the expectation that valuable information may be obtained. But many of these laboratory procedures result only in loss of time, energy and money, and the patient receives no benefit. Why encourage the use of such tests, which experience proves to be of doubtful, if any, value?

E. H. BOYER, M.D., Clinton, Iowa.

DRESSING FOR HEMATOMA OF EAR

To the Editor:—I was greatly interested in Dr. Ferguson's dressing for the ear (THE JOURNAL, March 11, p. 736). However, there are some cases which will not clear up under the best pressure treatment that can be devised. Recently a piano mover injured his ear, and a hematoma developed. I aspirated the blood and applied a pressure bandage with no success. I then incised the hematoma and removed all blood clots and irrigated the cavity with an antiseptic solution, but even this failed to cure the trouble. I therefore reopened the wound and packed the cavity of the hematoma with phenol (carbolic acid) on cotton. I had first, however, applied some sterile petrolatum about the opening of the cavity. After five minutes' application, I removed the phenol pack and applied a dressing to the ear. The next day the ear was rather inflamed and swollen. The inflammation and swelling soon subsided and the patient made an uneventful recovery with perfect results. I can recommend this treatment for those patients who are willing to bear a little pain to get a good cosmetic result.

NATHAN STEINBERG, M.D., Philadelphia.

NARCOLEPSY IN THE PICKWICKIAN SENSE

To the Editor:—The portrayal of the symptoms of a disease in a fictional character is always interesting reading. This is particularly true if the novel appeared before the malady was studied systematically or recorded authoritatively in the medical literature. An example of this kind occurs in Charles Dickens's Pickwick Papers. In a humorous character sketch, Dickens portrayed the symptoms of narcolepsy forty years before the publication of its first description as a clinical entity.

This disease, which physicians find fascinating because of its rarity and extraordinary manifestations, was described in 1877 by Westphal. He has properly received the credit attached to priority, although it was not until three years later that Gélineau first applied the term narcolepsy as a name for brief and sudden attacks of irresistible sleep. One of his patients had some two hundred attacks a day, each lasting from one to five minutes. Sir William Gowers described a similar case in a young girl of twenty-two and observed that if she yielded immediately to the inclination to sleep, the attack did not last more than about five minutes; but if she struggled to keep awake, sleep always conquered in a short time and lasted longer, ten or fifteen minutes. Gowers emphasized the rareness of these cases and insisted that they should not be confused with hysteria, "sleeping sickness" or minor epilepsy. More dramatic illustrations of the affliction are given by Perrier, whose patient, a soldier, went to sleep on guard duty, and by Spiller, who tells of a fireman sleeping while holding the grabirons of a locomotive traveling about seventy miles an hour. An eight year old girl, reported by Dr. Weech, fell asleep in the waiting room of a noisy hospital clinic and again on the examining table. She also displayed the "emotional asthenia" which Weech regards as essential to the diagnosis of true narcolepsy. Emotional states, such as laughing or crying, resulted in the production of a sudden overwhelming feeling of weakness and a general loss of muscular power. Similar ailments classified as symptomatic narcolepsy may accompany obesity, cerebral tumors, severe circulatory disorders, encephalitis, epilepsy and hysteria. The etiology, though unproved, probably depends on a localized injury of the brain.

Without available medical publications concerning this disease, the publication of Pickwick Papers in the year 1837 illustrates Dickens's acute powers of observation, as well as his lively sense of humor. The individual whose traits of character are modified by the symptoms of narcolepsy is Mr. Wardle's servant, generally spoken of as "Joe, the fat boy." The following unrelated sentences from the fourth chapter have been chosen as most likely to present an adequate description of his chief characteristics.

. . . and on the box sat a fat and red-faced boy, in a state of somnolency, whom no speculative observer could have regarded for an instant without setting down as the official dispenser of the contents of the before mentioned hamper, when the proper time for their consumption should arrive.

"Joe—damn that boy, he's gone to sleep again!"

Mr. Winkle mounted to the box, the fat boy waddled to the same perch, and fell fast asleep instantly.

"Joe, Joe" said the stout gentleman—"Damn that boy, he's gone to sleep again. Be good enough to pinch him, Sir—in the leg, if you please; nothing else wakes him—thank you. Undo the hamper, Joe."

"Plates, Joe, plates."

"Now, Joe, the fowls. Damn that boy; he's gone to sleep again. Joe! Joe!" (Sundry taps on the head with a stick, and the fat boy, with some difficulty, roused from his lethargy).

"Damn that boy," said the old gentleman, "he's gone to sleep again."

"Very extraordinary boy, that," said Mr. Pickwick, "does he always sleep in this way?"

"Sleep!" said the old gentleman, "he's always asleep. Goes on errands fast asleep and snores as he waits at table."

"How very odd!" said Mr. Pickwick.

"Oh! odd indeed," returned the old gentleman, "Im proud of the boy—wouldn't part with him on any account—damme, he's a natural curiosity! Here, Joe—Joe—take these things away, and open another bottle—d'ye hear?"

The fat boy arose, opened his eyes, swallowed the huge piece of pie he had been in the act of masticating when he last fell asleep, and slowly obeyed his master's orders.

As the Pickwickians turned round to take a last glimpse of it, the setting sun cast a rich glow on the faces of their entertainers, and fell upon the form of the fat boy. His head was sunk upon his bosom; and he slumbered again.

The absence of the early history makes it difficult to be certain that this was a genuine case of true narcolepsy. The association with obesity is significant. To snore as he waits at table may represent an exaggeration on the part of Mr. Wardle, but to fall asleep while eating leaves little doubt concerning the nature of the condition. There is no mention of emotional asthenia associated with the attacks. On the contrary, Joe exhibited considerable poise as the unseen witness of Mr. Tupman's amorous activities, although this scene may have been less strongly emotional than the reactions of the participants indicated.

PHILLIP E. ROTHMAN, M.D., Los Angeles.

"DOES PRIMARY TUBERCULOUS INFECTION AFFORD ADEQUATE PROTECTION AGAINST CONSUMPTION?"

To the Editor:—In THE JOURNAL, April 8, appeared an article with this title by Dr. Chester A. Stewart of Minneapolis. Any attempt at evaluating the interesting material presented should not overlook the fact that certain groups have parted ways with the fundamentalists in phthisiology by rejoining the ranks left meager by the virtual abandonment of the contagionist's attitude toward tuberculosis of a few decades ago.

In view of the continuation of the downward trend, since the late period of the eighteenth century, of the mortality curve from tuberculosis, I believe that it is an unwarranted nullification of the program of public education, from which so much benefit has been derived, to propagandize in favor of the high contagiousness of tuberculosis, especially since there are many of that school who find it necessary or expedient to teach that primary infection by tubercle bacilli, as manifested by the cutaneous allergic response to tuberculin, is tantamount to tuberculous manifest disease.

A return to the use of the word "consumption," in referring to manifest tuberculous disease of whatever stage, certainly serves to frighten many into accepting such theories that "primary tuberculous infections are distinctly detrimental," "observations indicate that first infections by Mycobacterium tuberculosis alter the normal state of resistance possessed by the uninfected body in such a manner that . . . the patient is doomed thereafter to have [consumption and the like] develop, if successfully reinfected," and that there may exist, without confirmatory evidence, one or more foci of indirect primary disease from which no separation into observation or manifest disease should be made.

As most adults have, have had or will have what the author considers "primary tuberculosis," demonstration of which primary infection by tubercle bacilli is recognized in the specific allergic skin reaction, yet with only small prospect of having such so-called primary tuberculosis result in any clinical or manifest disease, I feel strongly that, for the time being, or at least until some refuting scientific data are at hand, the accepted term "primary infection" should not be replaced by any such term as would imply that manifest disease had already become established at the time of first infection, such as in syphilis, and that treatment must therefore be definitely instituted.

The preponderance of existing evidence rests on the side of those who, like Heimbeck and a host of others, find a relative, though not absolute, immunity to tuberculous disease among allergic adults.

We should adhere, for the present, to the recently established Diagnostic Aids—Childhood Type of Tuberculosis as approved by the Committee on Childhood Tuberculosis of the American Sanatorium Association as furnishing a classification as satisfactory as any of the series of events which may follow a primary parenchymal infection by tubercle bacilli.

It is well, however, to continue studies that seek to trace the pathways to, and responsible factors for, resultant tuberculous disease among the relative few out of the great numbers who have experienced primary or simple infections.

Esmond R. Long, in a recent article, presented the stand that should be adopted at this time: "Certain groups [have] the conviction that, so far from being a factor in resistance, allergy is a dangerous state predisposing to destructive disease. As a matter of fact, no such dogmatic principles can be laid down, and . . . one of the praiseworthy modern trends in immunological theory in tuberculosis is [by] not attempting to explain any case in terms of sweeping generalizations." D. O. N. LINDBERG, M.D., Decatur, Ill.
Medical Director, Macon County
Tuberculosis Sanatorium.

DOSAGE OF REDUCED IRON

To the Editor:—My attention has been called, particularly by Dr. Marie L. Carns of Madison, Wis., to an error in my recent article on "Primary Hypochromic Anemia," which appeared in THE JOURNAL, February 25. I implied that reduced iron was ferrous oxide (FeO) and that its actual iron content was 78 per cent. This is incorrect. Reduced iron is metallic iron which has been produced by hydrogenating ferrous oxide, the resultant material being almost pure metallic iron, containing from 90 to 100 per cent of that metal. I have used this preparation in capsules containing 1 Gm. (15 grains), the daily dosage being from 3 to 6 Gm. The actual iron content at this dosage is extremely high, from 3,000 to 6,000 mg. of iron. It is probably necessary to use this large amount of actual iron because of the insolubility of the preparation. I have not found it necessary to use hydrochloric acid in conjunction with reduced iron even in those cases showing complete achlorhydria.

WILLIAM DAMESHEK, M.D., Boston.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

SUDDEN DEATH IN INFANCY

To the Editor:—I have an interesting case to report. The other morning, January 13 (it was also Friday), I was called to see a baby that had died in its sleep. There was no evidence of suffocation or foul play. The baby was well nourished and well developed, and seemed to be perfectly happy and mentally alert, as much as a child of 5 months should be. I saw the child at 6:30 a. m., and rigor mortis had already set in as well as postmortem lividity. The only external abnormalities were a dulness about the size of a lemon, in the upper portion of the chest, more on the left side, and the cranium was very soft, there being no evidence of ossification. Even the mother had noticed this but did not realize that it was not natural even for infants. Autopsy revealed an enlarged thymus, 9 by 5.5 by 1.5 cm., overlapping the heart and extending down to the fourth intercostal space with a firm origin about the trachea and esophagus. The spleen possibly was slightly enlarged. No large glands could be felt in the mediastinum or elsewhere. The other organs were in order and no pathologic changes were found in any of them. On inquiring back into the history of the child I learned from the mother that her baby would not take the nipple but would eat with a spoon and choked a little on her milk. Otherwise she played with some neighbor children apparently in the best of health. I forgot to mention that there was a definite rosary on the ribs at the costal margins, although the infant had received cod liver oil since 2½ months of age. These bony prominences were especially noticeable along the under surface. Was this a case of simple thymus enlargement? Was it status lymphaticus? Was there a possibility, on account of the condition of the skull, for there to be some pathologic condition in the parathyroids? It was this condition of the cranium that is particularly interesting. I should like to hear from you as soon as it is possible. Please omit name.

M.D., Nebraska.

ANSWER.—Sudden death of infants is commonly ascribed to the presence of a large thymus, or to the condition known as status thymolymphaticus. It has been shown that enlargement of the thymus is compatible with perfect health; that in normal well developed infants the thymus tends to be large, whereas in weakly, atrophic or sick infants it diminishes in size. Only in exceptional cases has the thymus been shown to exert pressure on the trachea, bronchi, large vessels or underlying organs in sufficient degree to produce death. It has been suggested that the hyperplastic thymus produces a toxic chemical substance. This is purely conjectural and there is no proof as to the nature or action of such a substance if it exists at all. If the thymus produces sudden death, what is the explanation of its mode of action? The same question may be asked with reference to status thymolymphaticus. The whole question of thymus death cannot be answered satisfactorily at the present time. The true physiology and the function of the thymus gland is far from being understood. Hammar, who has studied this organ for fifty years, is still not clear as to its function. Some of the deaths supposed to have been due to thymus hyperplasia have on closer investigation been found to be caused by infection, the aspiration of food particles into the bronchi and lungs. Infantile tetany is said to cause sudden death occasionally by producing cardiac arrest in systole. None of these assumptions explain all the sudden deaths of infancy.

Answering specifically the questions submitted:

1. The thymus was large, but it has been shown that the thymus varies in size under normal conditions for children of the same age; it is large and heavy in well developed children, and atrophies rapidly in weakly and sick children. Whether the thymus caused sudden death is difficult or impossible to prove in the light of our present knowledge and the subject is controversial. Many well informed students of this phase of pathology would be disinclined to make an affirmative statement.

2. There is no evidence of the existence of status thymolymphaticus in this infant. This condition implies a universal hyperplasia of lymphatic structures, including the spleen, regional lymph nodes and the lymphoid tissue of the gastrointestinal tract. No mention of such pathologic changes is contained in the autopsy report.

3. The soft condition of the cranial bones was undoubtedly due to craniotabes, which according to most investigators is a manifestation of rickets. However, a smaller group of observers maintain that the softening occurring in premature and some new-born infants is due to osteoporosis, the cause and nature of which is obscure.

The manifestations of parathyroid gland deficiency are characterized by low blood calcium, tetany and usually associated

rickets. In order to prove a parathyroid dysfunction it would be necessary to have evidence of the presence of the factors mentioned.

INTERPRETATION OF MANTOUX TEST IN TUBERCULOSIS

To the Editor:—I have been giving the Mantoux test to the children of Jefferson County School and to date have done 1,500 tests, with a positive reaction in 14 per cent of the children tested. About 1 per cent so far show activity. Some of the children have had severe local reactions and this seemed to be the case in those who are healthiest. Children whose general appearance shows them to be very much under par physically show a weaker reaction and the reactions in two brothers (out of four brothers to whom I gave the test last spring) were negative while the other healthier looking brothers showed a positive reaction. I have had one of these that showed a negative reaction in bed for three months with active tuberculosis. In another case which showed a very positive reaction the roentgenologist reported a negative or normal chest picture. I am anxious to know whether or not the severity of the reaction shows greater immunity than in the less severe. Of course I know that the children with active tuberculosis may be so toxic that the Mantoux test will be negative. In adults would a severe reaction show a healed chest condition or not? Any further information you can give me in regard to tuberculosis in children and the interpretation of the reaction to the Mantoux test will be greatly appreciated.

JAMES D. BLEVINS, M.D., Beaumont, Texas.

ANSWER.—Regarding the children mentioned, it seems that the one with tuberculosis must have been in an anergic state as a result of an overwhelming infection. Otherwise, with good technic and good tuberculin the reaction is roughly proportionate to the quantity of sensitizing antigen bathing the tissues. This in turn is dependent roughly on the size of the combined lesions, up to the point of overwhelming the body tissues. It does not necessarily mean that the immunity increases in proportion to the reaction, which is largely a hypersensitiveness. A certain degree of "immunity" or protective power accompanies this hypersensitiveness, or "allergy," as some term it, yet in large doses it may produce such an overwhelming response that the result is an exudative lesion of greater proportions than would result in a less sensitive person. A moderate sized lesion healing or active in an otherwise healthy child would tend to respond to the maximum, not only because of the presence of sensitizing antigen but also because the cells of the host are in a proper state of health and nourishment to give such a response. A roentgen examination is of no value if negative. Only about 50 per cent of healing primary lesions can be seen by this means.

In adults a severe reaction may show either an active lesion or a quiescent lesion (one that is partially encapsulated but still liberates toxins). It is of little value in a diagnosis or prognosis of either type. In latent and healed lesions, however, recent opinion seems to incline to a belief in a parallel disappearance of the tuberculin reaction with living tubercle bacilli. If not simultaneously, the disappearance follows soon in the wake of bacillary destruction.

PREMATURE ORGASM

To the Editor:—In THE JOURNAL, January 21, page 210, delayed orgasm was discussed. What treatment is suggested for the opposite condition, premature orgasm, other than the possible injection of a mild solution of cocaine? Is the latter a safe procedure? If so, how may it best be accomplished and what strength solution should be employed? Your terse, cryptic answers are often highly instructive and save much time. Please omit name.

M.D., Maryland.

ANSWER.—Leaving out of consideration the purely psychic cases, which probably constitute the majority and which may be controlled by psychotherapy, the condition of rapid orgasm may be due to one of two distinct pathologic conditions, and it is absolutely essential to make a correct differential diagnosis, as the treatment is entirely different for each cause. The first condition is one of irritability of the prostate and prostatic urethra due to congestion of these parts. In these cases the rapid orgasm is due to the fact that the reflex act of coitus, owing to the congestion already present, takes place at once with the added congestion of beginning coitus. This condition may be likened to a congestion of the nose wherein the slightest current of air will produce the reflex act of sneezing, whereas the normal nose will stand severe currents of air without sneezing. The treatment of this condition is to get rid of the local pathologic congestions by the use of gentle prostatic massage every five days and instillations of weak (from 1:3,000 to 1:500) silver nitrate solutions into the prostatic urethra with the Bangs sound syringe.

The second cause for rapid orgasm is a weakening of all the muscles connected with the sexual act. Around each vein in the penis is a muscular band whose function it is to contract and remain contracted for a sufficient period of time, so that the blood that has entered the penis by the dilated arteries shall not be permitted to escape through the veins but shall remain in the penis, thus giving it its rigidity. If these muscles are weak and relax too soon, the blood will flow out of the penis too quickly, with a consequent rapid end of the coital act. The treatment is a stimulation of all these muscles, and this is best accomplished by the use of the sinusoidal-faradic current of moderate rapidity and as strong as the patient can bear without any pain. One cable is connected with a rectal electrode and the other with a wet-sponge electrode applied to the perineum, and the current is allowed to pass for about ten minutes. Treatments may be given every three or four days till the patient is well. The use of cocaine in either of these conditions is unpractical and dangerous. It has to be given within a half hour of coitus and into the prostatic urethra, and there are cases of marked idiosyncrasy in which even weak solutions given in this way have caused serious symptoms of cocaine poisoning.

MYELITIS AFTER SPINAL ANESTHESIA

To the Editor:—Kindly discuss the changes in a case of myelitis due to spinal anesthesia. What is the treatment? What is the prognosis? Please omit name.

M.D., Georgia.

ANSWER.—Various kinds of cord lesions may follow spinal anesthesia, such as conus lesion with retention of urine and feces and painful anesthesia about the anus, as reported by J. Boisseau (*Rev. neurol.* **1**:1148 [June] 1930). In this case all treatment, including radiotherapy and epidural injection of iodized oil, proved futile. J. Michelsen (*München. med. Wchnschr.* **79**:1148 [July 15] 1932) has devoted an article to the cord lesions following spinal anesthesia. To our knowledge the worst case of all is described by Nonne and Demme (*Wien. klin. Wchnschr.* **41**:1002 [July 12] 1928) after herniotomy, with death after sixteen months. Conus myelitis, delicate adhesions between the cord and the thickened dura, and ascending cord degeneration were found post mortem. The treatment must necessarily vary in different cases according to the symptoms present, and no general rules can be laid down. Further data regarding the nervous complications of spinal anesthesia are given by F. G. Lindemulder (THE JOURNAL, July 16, 1932, p. 210) and by Davis, Haven, Givens and Emmett (THE JOURNAL, Dec. 12, 1931, p. 1781).

SODIUM ION MOST HARMFUL IN HYPERTENSION

To the Editor:—In Queries and Minor Notes (THE JOURNAL, January 14), Louis L. Sherman, M.D., of Oakland, Calif., asks pointedly, "Is it the sodium or the chloride in table salt which does the harm to patients having high blood pressure?" This is an important point. I wish to repeat his question and I hope some one can give a definite and authoritative answer to it.

VERNON A. CHAPMAN, M.D., Milwaukee.

ANSWER.—A dogmatic answer to this question is impossible. As previously stated, there is no convincing evidence that either the sodium ion or chloride ion of table salt has any appreciable deleterious effect on arterial hypertension. As the question was asked specifically in connection with hypertension, and did not state whether renal impairment existed or not, the foregoing is the only statement justified. When renal functional impairment exists, either associated with or independent of arterial hypertension, the sodium ion is definitely the more injurious ion of sodium chloride.

ALBUMINURIA IN YOUNG ADULT

To the Editor:—Please suggest treatment in a young adult having a trace of albumin and a few casts in the urine, otherwise normal, noticed during an insurance examination. Low protein and salt reduction diet after reasonable time produced no improvement. Please omit name.

M.D., New York.

ANSWER.—The treatment of albuminuria with the presence of a few casts in the urine depends on an accurate diagnosis. The first to be considered is the functional orthostatic albuminuria.

These albuminurias are characterized by the intermittent presence of albumin in the urine, and also the absence of formed elements, such as casts and cells of various kinds. The morning urine passed before arising is usually free of albumin. It must be admitted that, in the orthostatic albuminuria, albumin may be constantly present and casts may be observed. The latter group is difficult to differentiate from a genuine nephritis.

In orthostatic albuminuria there is nearly always some deflection of the spine, usually a scoliosis in the dorsal or dorsolumbar regions. The treatment for this condition consists of

measures to correct the spinal deformity by exercise or appliances and to avoid overexercise and fatigue.

If there is no evidence of edema or hypertension, if there is complete absence of red blood cells in the urine, or if the kidney function test is normal, the blood nitrogen values are not increased above their normal figures and the urine is not concentrated, associated with high specific gravity, one may infer that the albuminuria with a few casts is not due to organic kidney disease but in all probability to an orthostatic albuminuria. It should be cautioned, however, that the latter diagnosis should not be made until most careful, thorough and repeated examinations have been made, in order that an organic lesion may be eliminated. If the lesion should prove to be organic in nature, general hygienic measures should be employed and a proper dietary regimen instituted with a scanty amount of protein and salt in the food.

If anemia is present, iron should be employed. If foci of infection are detected, they should be removed and treated.

CELLASIN IN DIABETES

To the Editor:—I am enclosing circular advertising material which I have been receiving from time to time advocating the use of "Cellasin" as a cure for diabetes mellitus. It occurs to me that the claims for this product are misleading, although the advocates are careful to state that it is a ferment but go further to state that by this means it is a "metabolic ferment." You are probably already aware of the existence of this product and the advertising campaign. I have not seen any comment in THE JOURNAL about it and thought perhaps it would be wise to bring it to your attention. In my diabetes service at the Leonard Hospital I have found several patients who have used this product on the advice of their family physicians and were led to believe that they could rely on it as a protection against the ravages of this disease. Perhaps you can find some way to discuss its merits in THE JOURNAL.

STEPHEN H. CURTIS, M.D., Troy, N. Y.

ANSWER.—A report on Cellasin was made by the Council on Pharmacy and Chemistry in 1908 (THE JOURNAL, Sept. 12, 1908, p. 931) and a second report was issued in 1909 (THE JOURNAL, Oct. 30, 1909, p. 1499). A note reviewing the Council's report was published in THE JOURNAL, July 4, 1924, page 58. The investigation of the Council brought out that Cellasin did not contain a ferment as claimed but a spore-producing bacterium which splits sucrose largely into lactic acid.

No acceptable evidence for the value of Cellasin in the treatment of diabetes appears to have been published. On the other hand, a report was received from one who has done much work bearing on metabolism, stating that he had made one careful metabolic experiment in the use of Cellasin in the treatment of diabetes mellitus. In this experiment the use of Cellasin had no beneficial effect on the patient's diabetes.

PROPHYLACTIC IN GONORRHEA

To the Editor:—1. Would a weekly injection of 2 per cent strong silver protein as a prophylactic for gonorrhea, in the male urethra over a period of one year or many months, be likely to produce strictures, in view of its highly irritating character? 2. Is it safe to use a triweekly injection of 1 per cent strong silver protein in the case of a man, having a chronic anterior urethritis for eight months, and who appears improved by such an injection? These injections produce no irritation as far as any subjective symptoms are concerned. Please omit name.

M.D., New York.

ANSWER.—1. A 2 per cent injection of strong silver protein used once a week for a year would probably not produce a stricture, but why not use a milder silver solution, such as mild silver protein?

2. It is safe enough to use a triweekly injection of 1 per cent solution of strong silver protein, but urethritis which does not clear up in eight months is evidently not being helped by the injection. Perhaps it is causing it to persist.

INJURY TO LIP DURING TOOTH EXTRACTION UNDER LOCAL ANESTHESIA

To the Editor:—My dentist extracted a boy's lower molar under procaine hydrochloride with epinephrine and soon the lower lip began to swell. In a few days a slow-healing ulcer developed on the lower lip. What was the modus operandi and can similar mishaps be avoided in the future? A colleague told him that he had had similar experiences.

M.D., Illinois.

ANSWER.—Because of lack of more detail, the question can hardly be answered. If the inferior alveolar and lingual nerves have been blocked, the lower lip must also have become anesthetized and under this anesthesia any form of injury, mechanical or thermic, may have occurred without the boy's notice. As the procaine-epinephrine anesthesia wears off in approximately two hours, a persistence of anesthesia and a lack of regeneration following the injury to the mucous membrane should point to a more permanent damage of the injected nerve. The size of the needle, an unusually large hematoma around the injection, or a faulty solution could all be considered.

A partial injury of the inferior alveolar nerve could have also occurred at the socket of the extracted tooth. Such partial nerve injuries are known to produce trophic changes. As there are no data concerning a hyperesthesia or paresthesia of the lower lip, this is only a conjecture.

NUMBNESS AND PAIN AFTER INJURY TO BRACHIAL PLEXUS

To the Editor:—A woman, aged 30, suffered a severe contusion of the right shoulder with fracture of the clavicle at the inner third. The fracture was wired. A severe hyperesthesia of the medial aspect of the arm, forearm, thumb and medial half of the first finger cleared after three months. The numbness and pain, however, have persisted, after two years, in the medial half of the terminal phalanx of the thumb. Please advise treatment and prognosis. Kindly omit name.

M.D., Ohio.

ANSWER.—There probably was an injury of the brachial plexus at the time of the fracture, with resulting fibrosis and scar tissue formation about it. The fact that pain and numbness persist after a period of two years indicates that the process of recovery has probably gone as far as it will go and that the symptoms still present are likely to persist unless the brachial plexus is carefully exposed and freed from the scar tissue which partially surrounds and compresses it. Needless to say, the operation is technically difficult and associated with a certain degree of risk. Whether or not it should be undertaken depends on the severity of symptoms and the disability which the symptoms produce.

PAIN IN TESTIS

To the Editor:—I have a patient concerning whom I wish to solicit your help, as I am unable to decide the source of his trouble. For the last five years he has had a dull ache in the left testicle at times amounting only to a consciousness of its presence and at other times increasing to slightly more severe. Following intercourse for the next day he is almost incapacitated with the increased intensity of the pain, which lasts about twenty-four hours, at which time it subsides to its usual slight aching character. He has no varicocele, the prostate seems normal, and the urine is normal. Can you offer any suggestions as to the diagnosis and treatment?

M.D., Wisconsin.

ANSWER.—Pain in the testicle aggravated by sexual intercourse is most frequently due to disease in the prostate gland or seminal vesicles or both. In order to exclude the adnexa as factors in the production of pain, it is most important to massage the prostate and vesicles and to examine the strippings obtained for the presence of pus. It is best in doubtful cases to examine the strippings for pus at least three times, preferably at weekly intervals. If examination of the prostate and vesicles gives negative results, it might be well to examine the patient's deep urethra with the urethroscope and, failing to find pathologic changes there, it might be well to examine him for the presence of a neuritis. However, the cause is most frequently found in the prostate and vesicles and the treatment, therefore, directed toward the treatment of infection in the prostate and vesicles; namely, (1) massage of the prostate and vesicles about once a week; (2) instillation of a 1 per cent solution of strong silver protein into the urethra after massage; (3) heat applied to the prostate and vesicles by rectum by means of any one of the well known devices for this purpose.

HARM IN EYE EXERCISES AND EYE MASSAGE

To the Editor:—Is eye exercise, eye massage, and the practice of central fixation by use of the Snellen test card of any value in the treatment of errors of refraction such as myopia and hyperopia? In your opinion would the practice of these have any injurious effects on the human ametropic eye or help produce any anatomic changes, such as detachment of the retina? What is the difference in length of the optical axis of an emmetropic eye and an ametropic eye with a myopia of 1 diopter? Please omit name.

M.D., Indiana.

ANSWER.—No. Eye exercise, eye massage, and central fixation of the Snellen or any other card are the hooks on which the modern ophthalmic quack impales his victims, aided by the lure of a lot of high-sounding hooey. Such practices cannot influence errors of refraction one iota in any respect, but eye exercises and eye massage can be most destructive in detachment of the retina and certain other conditions. Three diopters of myopia is equivalent to an increase in length of 1 millimeter; hence 1 diopter of myopia indicates an axial difference in length of approximately one-third millimeter.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

AMERICAN BOARD FOR OPHTHALMIC EXAMINATIONS: Milwaukee, June 12. Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: The *general oral, clinical and pathological* examination will be held in Milwaukee, June 13. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OTOLARYNGOLOGY: Milwaukee, June 12. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

ARKANSAS: *Regular.* Little Rock, May 9-10. Sec., Dr. Sam J. Allbright, Box 54, Searcy. *Eclectic.* Little Rock, May 9. Sec., Dr. Claude E. Laws, 803½ Garrison Ave., Fort Smith. *Homeopathic.* Little Rock, May 9. Sec., Dr. Allison A. Pringle, Eureka Springs.

CALIFORNIA: *Reciprocity.* San Francisco, June 14. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

CONNECTICUT: *Basic Science.* Prerequisite to license examination. New Haven, June 10. Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Wilmington, June 13-15. Sec., Dr. Harold L. Springer, 1013 Washington St., Wilmington.

FLORIDA: Jacksonville, June 12-13. Sec., Dr. William M. Rowlett, Box 786, Tampa.

IOWA: Iowa City, June 6-8. Dir., Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KENTUCKY: Louisville, June 7. Sec., Dr. A. T. McCormack, 532 W. Main St., Louisville.

MISSOURI: St. Louis, June 7-9. Sec., Dr. James Stewart, Capitol Bldg., Jefferson City.

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* The examinations will be held at centers where there are five or more candidates, May 8-10, June 26-28, and Sept. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

NEBRASKA: Omaha, June 7-9. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

OHIO: Columbus, June 6-9. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

WISCONSIN: *Basic Science.* Milwaukee, June 17. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Regular.* Milwaukee, June 27-29. Sec., Dr. Robert E. Flynn, 401 Main St., La Crosse.

WYOMING: Cheyenne, June 5. Sec., Dr. W. H. Hassed, Capitol Bldg., Cheyenne.

Hawaii January Report

Dr. James A. Morgan, secretary, Board of Medical Examiners, Territory of Hawaii, reports the written examination held in Honolulu, Jan. 9-12, 1933. The examination covered 10 subjects and included 55 questions. An average of 75 per cent was required to pass. One candidate was examined and passed. One physician was licensed by endorsement. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
Washington University School of Medicine		(1929)	80.3

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1932)	N. B. M. Ex.

Pennsylvania Reciprocity Report

Mr. Charles D. Koch, secretary, Pennsylvania State Board of Medical Education and Licensure, reports 5 physicians licensed by reciprocity with other states from Jan. 3 to Jan. 20, 1933. The following colleges were represented:

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Northwestern University Medical School		(1904)	Illinois
University of Maryland School of Medicine and College of Physicians and Surgeons		(1924)	Indiana
Detroit College of Medicine and Surgery		(1929)	Michigan
University of Minnesota Medical School		(1931)	Minnesota
Syracuse University College of Medicine		(1923)	New York

Alabama January Report

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports the written examination held in Montgomery, Jan. 10-13, 1933. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. Two physicians were licensed by reciprocity with other states from January 4 to January 9. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
University of Louisville School of Medicine		(1932)	81.9
University of Tennessee College of Medicine		(1932)	86.7

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Chicago Medical School		(1921)	Illinois
University of Pennsylvania School of Medicine		(1928)	Penna.

Book Notices

Asthma, Hay Fever and Related Disorders: A Guide for Patients. By Samuel M. Feinberg, M.D., F.A.C.P., Assistant Professor of Medicine and Attending Physician in Asthma and Hay Fever Clinic, Northwestern University Medical School. Cloth. Price, $1.50. Pp. 124, with 8 illustrations. Philadelphia: Lea & Febiger, 1933.

This is a readable book for sufferers from hay fever and asthma. It presents a distinct advantage in being free from discussion of the dangers and handicaps that overhang many of these patients, which of necessity must be described in books for the profession. The book contains an historical review of the subject, a description of the symptoms and mechanism of the disease, and a discussion of primary and secondary causes of the illness and of methods of examining and treatment which the hay fever patient should know in order to cooperate well with the physician. In the historical review, Feinberg states that "not until 1819 did John Bostock, himself a sufferer of the malady, describe hay fever as a definite medical entity." However, Bostock failed to appreciate the cause of the condition. "He said that summer catarrh was due to heat and the sun's rays." Why couldn't he have given Bostock credit for what he really said he discovered? The author mentions the fact that nasal operations should be taken only after all other measures have been used to relieve the malady. This might have been exphasized more heroically. He also mentions the need of caution about the use of serum in sufferers from hay fever or asthma. This should have been emphasized still more heroically, since the number of deaths reported from the use of serum in asthma patients is growing so steadily that its use in cases of allergy should be looked on as a greater hazard than a skull operation for brain tumor in a nonallergic case. He gives detailed descriptions of the use of epinephrine which every asthma patient should know and describes the use of symptomatic remedies and finally the necessity of the avoidance of "patent medicines," which contains nothing unknown to the medical profession at large. He finally urges against credence in the deceptive advertising of quacks. He might have urged with equal emphasis against credence in unwarranted and unsought for advice from friends and neighbors. Every asthma patient should be warned that free advice is worth exactly what it costs—not a cent.

Thérapeutique médicale. V: Peau, syphilis et cancer. Par MM. M. Loeper, G. Milian, L. Bory, Cl. Simon, A. Sézary, Ch. Flandin, H. Gougerot, M. Villaret, G. Roussy, E. Schulmann, R. Proust, E. Peyre, H. Rubens-Duval et Th. Alajouanine. Paper. Price, 50 francs. Pp. 408. Paris: Masson & Cie, 1932.

This small volume includes lectures, complementary to Loeper's course on therapeutics, given during 1932. In his discussion on skin infection, Milian deprecates the prolonged use of poultices, because of their tendency to give rise to and aggravate furunculosis, owing to maceration of the skin which they produce. In the treatment of pyodermatitis he prefers 1 per cent solution of iodine in alcohol applied twice daily. He also makes extensive use, in skin infection, of a 0.25 per cent solution each of methyl violet and methyl green in alcohol. In discussing the external remedies used in dermatoses, Bory points out that, in view of the richness of the epidermis in sulphur (2.48 per cent), it is no wonder that sulphur is one of the most important medicaments in dermatotherapy. He gives a formula for colloidal sulphur, prepared by boiling washed sulphur (0.20 Gm.) in glycerin (100 cc.) from three to five minutes (protected as much as possible against access of air), filtering while hot and then throwing it into distilled water 50 cc.). Bory is particularly fond of xylene, which he considers endowed with remarkable antiseptic and parasiticidal properties, as well as with stimulating qualities to epidermal reconstruction, in addition to being an excellent solvent. In superficial skin infections he employs from 0.5 to 1 per cent iodine dissolved in 10 per cent xylene, which is then incorporated in petrolatum or liquid petrolatum, the latter being used for applications to hairy parts. For the radical cure of sebaceous cysts he recommends a small incision to empty the contents after injection of a few drops of xylene. After reinjection of a few more drops to clean the cyst completely, a hot moist compress is applied to the flattened cyst. Clement Simon takes up general medication in dermatology. Sezary

contributes a practical exposition of the treatment of syphilis, which on the whole agrees with the methods employed in this country excepting that the French are more inclined than we to employ the subcutaneous or intramuscular injection of sulpharsphenamine, which, it is claimed, is better borne if dissolved in 4.7 per cent dextrose with 0.5 per cent phenol. The untoward effects of arsenotherapy are discussed by Flandin, while Gougerot takes up the prophylaxis of syphilis and Villaret the climatotherapy and balneotherapy. The treatment of cancer in general is the topic of Roussy. In the therapy of skin cancer, Schulmann emphasizes the treatment of precancerous lesions (such as nevi, xeroderma pigmentosum, Paget's and Bowen's disease, senile and presenile keratoses, arsenic and tar cancer, radiodermatitis, leukoplakia and erythroplakia) as well as the necessity for prompt and early treatment of actual cancers. He brings out strongly the curability of these lesions and the responsibility of the general practitioner in these cases. The book is concluded by Proust's short chapter on the therapy of internal cancers and articles by Peyre on experimental chemotherapy, Rubens-Duval on experimental biologic therapy of cancer, and Alajouanine on treatment of the pains of the cancer patient. It would indeed be desirable if such courses on therapy could be arranged for in this country to balance the other medical courses, which are generally deficient in therapeutics.

Calcium Metabolism and Calcium Therapy. By Abraham Cantarow, M.D., Instructor in Medicine, Jefferson Medical College. With a foreword by Robert Amory Hare, B.Sc., M.D., LL.D. Second edition. Fabrikoid. Price, $2.50. Pp. 252, with 3 illustrations. Philadelphia: Lea & Febiger, 1933.

The second edition of this valuable little book represents a distinctly successful attempt on the part of Dr. Cantarow to revise and supplement the material presented in the first edition. In order to keep pace with the numerous recent developments in the field of calcium metabolism and calcium therapy, a number of investigations which have shed light on certain controversial points have been embodied. The former belief that there exists an interrelationship between the action of the parathyroid hormone and that of vitamin D has been replaced by the view that these two substances act independently on calcium metabolism. Other new material presented in this edition includes the relation of the calcium and phosphorus intake to the effects of vitamin D and the parathyroid hormone; the nature of parathyroid action; the significance of phosphatases in the mechanism of ossification and in bone diseases; dental caries; the influence of calcium on the pharmacologic action of various drugs; and the in vivo diffusibility of calcium in nephritis with uremia and in parathyroprivic tetany. In view of the divergent current opinions regarding the etiology of dental caries, the author's apparent endorsement of the alleged definite relation between this obscure condition, calcium metabolism and vitamin D seems unwarranted. This book should prove particularly valuable to the clinician who desires a thorough and authoritative discussion of the values and limitations of calcium therapy.

Die Einteilung des Nervensystems nach seinen Leistungen. Von L. R. Müller, Professor der inneren Medizin in Erlangen. Boards. Price, 6.80 marks. Pp. 74, with 21 illustrations. Leipzig: Georg Thieme, 1933.

An attempt at a functional analysis of the brain is made in this brief monograph. Müller recognizes three principal subdivisions of the nervous system: (1) systema nervosum pro mundo, the division that receives stimuli from and reacts on the environment; (2) Systema nervosum myostaticum, receiving impulses from the vestibular labyrinth and from the muscle joints and tendons and sending impulses to the muscles for the maintenance of equilibrium, posture and tonus; (3) Systema nervosum vitale, concerned with the afferent and efferent innervation of the viscera, blood vessels, glands and the smooth muscle of the hair follicles. On the afferent side these divisions include, respectively, Sherrington's exteroceptive, proprioceptive and interoceptive sensory fibers and their nuclei of reception. On the efferent side, Müller's divisions 1 and 2 include the somatic motor elements, and division 3 the visceral efferent elements. An adequate discussion of the relation of the higher centers in the brain to these three afferent and two efferent divisions would require a large volume, and when this is attempted in seventy-four pages the result is necessarily disappointing. The incompleteness of the analysis will be evident from a glance at the three large colored drawings (figs. 1, 9 and 10) in which such important elements as the visual system, the vestibulospinal tract and the vagus nerves are omitted.

Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System. By Harvey Cushing. Cloth. Price, $5. Pp. 234, with 99 illustrations. Springfield, Ill.: Charles C. Thomas, 1932.

The publisher has incorporated four phases of Cushing's work in a beautifully printed and illustrated volume. Each section has formed the basis of an honorary lecture either at home or abroad and, being closely related, they form together a coherent volume. The first section deals with neurohypophyseal mechanisms from a clinical standpoint using the effects of hypophyseal tumors for the most part as evidence. Cushing believes that the hypophysis and diencephalon form a unit that functions as a whole. The next section concerns posterior pituitary hormone and the parasympathetic nervous system. Herein are reprinted the brilliant experiments concerned with observations on the effects of intraventricular injections of various drugs in conscious human beings. Cushing believes that a parasympathetic center resides in the diencephalon activated by posterior lobe secretion but that this secretion is itself under control by a neural mechanism situated in the tuber cinereum. The third section deals with pituitary basophilism, which Cushing clinically segregates from other obscure polyglandular syndromes. The author has adequate clinical evidence for a circumscribed syndrome and sufficient necropsy material for a firm conviction of its etiology. The last section is the most speculative and attempts to place the etiology of peptic ulcer on lesions of the diencephalon. The language in which the data are presented and the manner in which each subject is evolved into a firm argument make the book a literary as well as a scientific achievement. Even though some of the conclusions may not withstand the scrutiny of subsequent investigators, they form a source of stimulation to further work. The volume is recommended to all those interested in the nervous system and metabolic functions.

Handbuch der mikroskopischen Anatomie des Menschen. Herausgegeben von Wilhelm v. Möllendorff. Band V: Verdauungsapparat. Teil 2: Magen, Leber, Gallenwege. Bearbeitet von W. Pfuhl und H. Plenk. Paper. Price, 110 marks. Pp. 489, with 254 illustrations. Berlin: Julius Springer, 1932.

Plenk, in his admirable chapter on the stomach, acknowledges much help from the preliminary work done on it by Josef Lehner. Proceeding from the relations as found in man, he considers the homologies of the various regions of the stomach in different vertebrates, with particular emphasis on mammals. Such comparative data are essential for the interpretation of experimental work and help to differentiate fundamental from incidental conditions. Occasionally they illustrate general principles. Thus, the presence of striated muscle throughout the gastro-intestinal tract of certain fishes shows that the difference between smooth and striated muscle is essentially a physiologic and not a morphologic one. New data are presented on the histogenesis of the stomach in man and on its regenerative capacities. The critical discussion of the histophysiology of the cell types in the gastric glands is in agreement with the recent exposition by Bensley. The small number of normal human gastric mucous membranes that have been studied gives especial importance to the new material here described. The bibliography is as complete and as free from errors as could possibly be expected. Pfuhl, in his chapter on the liver, has omitted some important work, but he was confronted by a vast literature. His presentation is also essentially physiologic and has much that is new in it. A brief survey of the development is followed by a description of the lobulation and the evidence that this is the result of the postnatal equalizing of the vascular pressures in the arterial and venous channels which becomes necessary when respiration starts. There is a good presentation of the normal and experimental work on the organelles, the glycogen and the lipoids of the hepatic cell. The question is raised as to the effects of emotional states on these labile cells. The importance of postmortem changes is stressed. The incompleteness of many legends is annoying, for it is necessary to know the method of preparation and the lenses used in the study of cytologic material if one is to evaluate an illustration. The problems of the stellate cells are considered in all detail and there is a good account of the

histophysiology of the gallbladder. This handbook is indispensable for all histologists and pathologists, but at present there are few who can have the work on their own shelves. Its value and influence would unquestionably be increased if the price were reduced and in the long run the publishers would profit.

Anatomie humaine: Descriptive et topographique. Par H. Rouvière, professeur d'anatomie à la Faculté de médecine de Paris. Tome I: Tête. cou et tronc. (En deux fascicules.) Tome II: Membres, système nerveux central. Third edition. Cloth. Price, 400 francs per set. Pp. 1112, with 610 illustrations; 692, with 498 illustrations. Paris: Masson & Cie, 1932.

This edition of Rouvière's well known textbook of gross anatomy presents considerable changes. Certain chapters, particularly those dealing with the lymphatic and sympathetic nervous systems, have been entirely revised. More than a hundred new illustrations have been added, and the topographical anatomy of the abdominal wall has been completed by a brief description of the spinal and lumbo-iliac regions. Improvements in the presentation of some of the subjects has enabled the author to increase the size of the work no more than a hundred and thirty pages, in spite of the additional illustrations. Rouvière's Anatomy has always been a favorite French textbook for medical students, and for American students who prefer a French textbook this work is probably the most favorable one to recommend. The work remains as before, divided into three convenient volumes: one on the head and neck, one on the trunk, and one on the limbs. The illustrations are for the most part halftone reproductions on glossy paper, and the typography is excellent. The number and quality of the illustrations are probably superior to those of some of American textbooks.

The Purchase of Medical Care Through Fixed Periodic Payment. By Pierce Williams, of the Staff of the National Bureau of Economic Research, Inc. Assisted by Isabel C. Chamberlain. (Publications of the National Bureau of Economic Research, Inc., No. 20). Cloth. Price, $3. Pp. 308. New York: National Bureau of Economic Research, Inc., 1932.

This is a compilation of the methods used, chiefly by railroads and various lumber and mining industries, to provide medical care for employees at fixed periodic payments. It is useful as showing the extent to which contract practice has been carried in many sections of the United States. Although the author makes specific reference to many organizations using various types of contract practice methods, he omits specific reference in many places where they would be most helpful. No reference is made to the quality of medical care given the employees or members of contract covered groups. The general tone of the report leads the reader to assume that there is no question as to the quality of medical service. The organization and administration of these fixed payment plans is described in a very favorable tone and omits any criticism or analysis of the dangerous and undesirable features. The general tone of the work gives one the impression that the purpose is to defend the fixed periodic payment method and to convert the reader to the support of such plans.

Les séquelles de l'encéphalite épidémique: Etude clinique et thérapeutique. Par Georges Guillain, professeur de clinique des maladies du système nerveux à la Faculté de médecine de Paris, et Pierre Mollaret, chef de clinique à la Faculté de médecine de Paris. La pratique médicale illustrée. Directeurs, Professeur E. Sergent, R. Mignot et R. Turpin. Paper. Price, 28 francs. Pp. 106, with 21 illustrations. Paris: G. Doin & Cie, 1932.

This monograph on the late stages of epidemic encephalitis belongs in the large series known as "La pratique médicale illustrée" edited by Sergent, Mignot and Turpin. It is based on the extensive personal experience of the authors and on quite complete study of the literature, both French and foreign. There are chapters on the parkinsonian syndrome, dystonias, abnormal movements, sensory disturbances, vegetative disorders, psychic disorders, clinical forms, diagnosis and treatment. Each subject is necessarily treated in a condensed manner but with only few omissions of data of any importance, as, for instance, when it is stated (page 64) that modifications of basal metabolism have not been observed in the various post-encephalitic syndromes, though decided modifications were observed in twenty-eight of forty-seven cases reported from America by Naccarati in 1926. The book deals entirely with the clinical side, including treatment; the pathology is not discussed.

A Manual of Bacteriology, Medical and Applied. By R. Tanner Hewlett, M.D., F.R.C.P., D.P.H., Director of Pathology, Seamen's Hospital, Greenwich, and James McIntosh, M.D., B.Ch., Professor of Pathology, University of London. Ninth edition. Cloth. Price, 18s. Pp. 746, with 109 illustrations. London: J. & A. Churchill, 1932.

The authors, in this revision, have effectively incorporated the newer concepts in the field of pathogenic microbiology. They present many topics of a wide range of interest, which is made possible only by the concise but pleasantly readable style; numerous well chosen references indicate direction for further study. On the other hand, material is selected, as problems of general biologic interest are only briefly discussed or are omitted. The action of the infectious agent is frequently correlated with the pathologic process in the host, and laboratory procedures and methods of bacterial identification are well described. The illustrations leave little to be desired in presenting microscopic forms both in culture and in pathologic material. The book is admirably suited for a textbook for the student in pathogenic bacteriology and parasitology, and its few faults are attributable to brevity.

Medicolegal

Negligence of Sanipractor in Treating Fracture

(Sears v. Lydon, Sears et ux. v. Lydon (Wash.), 13 P. (2d) 475)

The defendant, a licensed sanipractor, attended Mrs. Sears in labor. Twins were born. The second child descended in a transverse presentation, the left arm preceding the head and trunk. After several unsuccessful attempts to replace the arm and shift the fetal body, the defendant sanipractor effected delivery by pulling on the protruding arm, but the arm was broken in the procedure. The sanipractor's treatment of the fracture was unsuccessful, blood poisoning set in, and later, to save the baby's life, a physician amputated the arm near the shoulder.

Two suits for malpractice were brought against the defendant, one by the child's guardian ad litem and one by the parents, but both suits were consolidated for trial. The complaints in both cases charged negligence in the treatment of the fracture, but were silent concerning the manner of delivery and the breaking of the arm. They alleged that the defendant bound the arm so tightly with nonelastic adhesive tape as to prevent the circulation of the blood and that he thereafter negligently failed to inspect and loosen the bandages, as a result of which blood poison developed. The plaintiffs introduced evidence that the condition of the baby's fingers and hand grew steadily worse after the fracture was set. After nine days the condition became so alarming that the defendant sanipractor, after removing a part of the bandages, advised that the baby be taken to a hospital. A physician testified that he examined the baby at the hospital and found, on removing the bandages, that the arm had been bound so tightly that three splints made of tongue depressors had sunk into the flesh and left distinct marks when removed; that the arm was then dead from about two or three inches below the shoulder downward; that gangrene had set in, and that an amputation was necessary to save the child's life. The defendant insisted that he had wrapped the arm in antiseptic gauze and cotton and bound pieces of yucca board around it to hold the arm in normal position, that he had not used tongue depressors, and that the bandages had been tampered with by the parents. He asserted that on several visits he noticed that the wrappings had been altered but said nothing to the parents about it; that from the beginning the fingers showed blue spots about the nails and that as the days passed these marks turned to gray, indicating an improvement in circulation. The jury returned verdicts for the plaintiffs, and the sanipractor appealed to the Supreme Court of Washington.

The defendant sanipractor assigned error in an instruction given the jury in which it was told that if a physician holds himself out as having special knowledge or skill in the reduction and treatment of fractures, then he is required to possess that knowledge and degree of skill usually possessed by specialists in that line of practice, in the same or similar communities, and that if he fails to possess that knowledge and skill, or if,

possessing it, he fails to exercise it with reasonable care, he is guilty of negligence. The defendant contended that this instruction assumed that he was to be judged as to his qualifications as a specialist without regard to the school of healing to which he belonged, and that it assumed also that he held himself out as a specialist in the reduction of fractures. The general rule for which the defendant contends, said the Supreme Court, is no doubt correct, but here the defendant testified that he was an expert in bone surgery and that he so represented himself to the child's father at the time of undertaking to reduce the fracture. He further testified that the method he employed was the one followed by "the schools generally of practitioners in the general practice" and advocated by standard written authority. There was no evidence that the defendant in reducing the fracture employed a method peculiar to his own school of healing or different from that employed by physicians in general practice. Under the evidence, the instruction was proper.

The defendant further complained that the trial court refused to instruct the jury to limit the damages to the result of negligence in binding the arm too tightly and not giving it proper treatment and to exclude any recovery for injury resulting from the manner in which he effected the transverse delivery. Under the pleading, said the Supreme Court, and under the evidence introduced by the plaintiffs, such an instruction would have been entirely proper, to prevent confusing the jury as to the exact issues before it. The plaintiffs did not claim, nor introduce evidence to prove, that the defendant was liable for the original fracture. But the defendant himself, not content with the limited issues so presented, sought to fortify his position by advancing a theory that contained the germ of an additional issue, namely, that of original negligence in the delivery, causing the fracture of the arm. He testified that the fracture could not possibly have been avoided. The plaintiffs accepted the challenge the defendant himself thus offered them, and on cross-examination and in rebuttal, they adduced evidence from which the jury was reasonably entitled to infer that the negligence of the defendant preceded the attempted reduction of the fracture and lay in the manner of delivery. All this evidence, on both sides, went to the jury wholly without objection. The defendant having invited the contest on a new field—in fact, having chosen the ground himself—cannot be heard to say that the jury should not have been allowed to determine that issue. Had the plaintiffs themselves attempted to open that field of inquiry, an objection by the defendant would have been properly sustained, but the defendant cannot on the one hand erect a barrier of defense and on another brush it aside. The defendant's contention, if followed to its logical conclusion, would enable a defendant to admit or to establish a distinct act of negligence on his part, other than that with which the plaintiff charged him, and then to escape the consequences of that negligence on the ground that it had not been specifically alleged by the plaintiff. To permit such a course of procedure would be unreasonable and unjust.

For the reasons stated above, the judgments in favor of the plaintiffs were affirmed.

Workmen's Compensation Acts: Injury Aggravated by Disregard of Physician's Advice.—A workman injured in the course of his employment, says the Supreme Court of South Dakota, cannot recover compensation for an increase of disability, due to his failure to use ordinary care to avoid aggravating the injury. An injury aggravated or extended in time by the employee's neglect or disobedience of his physician's instructions is not compensable as to the additional period of disability. Here an employee suffered an injury to his back. He was taken to a hospital and left on the fifth day without the permission of his attending physician. The physician advised him to wear a brace and to have a certain operation performed on his back. He would not consent to the operation and did not wear the brace. At various times he did heavy work, went to dances and became intoxicated. Physicians who had examined the employee were of the opinion that the employee by his conduct and by his disregard of advice and instructions had probably aggravated his injury and that had he obeyed his physician's instructions he probably would have been cured by the time of the hearing.—*Detling v. Tessier (S. D.), 244 N. W. 538.*

Society Proceedings

COMING MEETINGS

American Medical Association, Milwaukee, June 12-16. Dr. Olin West, 535 North Dearborn Street, Chicago, Secretary.

American Academy of Pediatrics, Chicago, June 12-13. Dr. Clifford G. Grulee, 636 Church Street, Evanston, Ill., Secretary.

American Association for the Study of Goiter, Memphis, Tenn., May 15-17. Dr. J. R. Yung, 670 Cherry Street, Terre Haute, Ind., Secretary.

American Association for the Study of the Feeble-Minded, Boston, May 31-June 3. Dr. Groves B. Smith, Beverly Farms, Godfrey, Ill., Secretary.

American Association for Thoracic Surgery, Washington, D. C., May 9-11. Dr. Duff S. Allen, 3720 Washington Boulevard, St. Louis, Secretary.

American Association of Genito-Urinary Surgeons, Washington, D. C., May 8-10. Dr. Henry L. Sanford, 1621 Euclid Avenue, Cleveland, Secretary.

American Association of Medical Milk Commissions, Milwaukee, June 12-13. Dr. Harris Moak, 360 Park Place, Brooklyn, Secretary.

American Association of Pathologists and Bacteriologists, Washington, D. C., May 2-3. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Bronchoscopic Society, Washington, D. C., May 10. Dr. Edwin McGinnis, 104 South Michigan Boulevard, Chicago, Secretary.

American Climatological and Clinical Association, Washington, D. C., May 9-10. Arthur K. Stone, Auburn Street, Framingham Center, Massachusetts, Secretary.

American Dermatological Association, Chicago, June 8-10. Dr. W. H. Guy, 500 Penn Avenue, Pittsburgh, Secretary.

American Gastro-Enterological Association, Washington, D. C., May 8-9. Dr. John Bryant, 311 Beacon Street, Boston, Acting Secretary.

American Gynecological Society, Washington, D. C., May 8-10. Dr. Otto H. Schwarz, 636 South Kingshighway, St. Louis, Secretary.

American Laryngological Association, Washington, D. C., May 9-10. Dr. George M. Coates, 1721 Pine Street, Philadelphia, Secretary.

American Laryngological, Rhinological and Otological Society, Chicago, June 8-10. Dr. Robert L. Loughran, 33 East 63d Street, New York, Secretary.

American Neurological Association, Washington, D. C., May 9-11. Dr. Henry A. Riley, 117 East 72d Street, New York, Secretary.

American Ophthalmological Society, Washington, D. C., May 8-10. Dr. J. Milton Griscom, 2213 Walnut Street, Philadelphia, Secretary.

American Orthopedic Association, Washington, D. C., May 8-10. Dr. DeForest P. Willard, 1916 Spruce Street, Philadelphia, Secretary.

American Otological Society, Washington, D. C., May 8-9. Dr. Thomas J. Harris, 104 East 40th Street, New York, Secretary.

American Pediatric Society, Washington, D. C., May 8-10. Dr. Hugh McCulloch, 325 North Euclid Avenue, St. Louis, Secretary.

American Proctologic Society, Chicago, June 12-13. Dr. Frank G. Runyeon, 1361 Perkiomen Avenue, Reading, Pa., Secretary.

American Psychiatric Association, Boston, May 29-June 2. Dr. Clarence O. Cheney, 722 West 168th Street, New York, Secretary.

American Society for Clinical Investigation, Washington, D. C., May 8. Dr. H. L. Blumgart, Beth Israel Hospital, Boston, Secretary.

American Society of Clinical Pathologists, Milwaukee, June 9-12. Dr. A. S. Giordano, 531 North Main Street, South Bend, Ind., Secretary.

American Surgical Association, Washington, D. C., May 8-10. Dr. Vernon C. David, 59 East Madison Street, Chicago, Secretary.

American Urological Association, Chicago, June 20-22. Dr. Gilbert J. Thomas, 1009 Nicollet Avenue, Minneapolis, Secretary.

Arkansas Medical Society, Hot Springs, May 2-4. Dr. William R. Barrar, 213 West Second Street, Little Rock, Secretary.

Association for the Study of Allergy, Milwaukee, June 12-13. Dr. Warren T. Vaughan, 808 Professional Building, Richmond, Va., Secretary.

Association for the Study of Internal Secretions, Milwaukee, June 12-13. Dr. F. M. Pottenger, 1930 Wilshire Boulevard, Los Angeles, Secretary.

Association of American Physicians, Washington, D. C., May 9-10. Dr. James H. Means, Massachusetts General Hospital, Boston, Secretary.

Conference of State and Provincial Health Authorities, Washington, D. C., June 5-6. Dr. A. J. Chesley, State Department of Health, St. Paul, Secretary.

Congress of Physicians and Surgeons of North America, Washington, D. C., May 9-10. Dr. John T. King, Jr., 1210 Eutaw Place, Baltimore, Secretary.

Connecticut State Medical Society, Hartford, May 24-25. Dr. Charles W. Comfort, Jr., 27 Elm Street, New Haven, Secretary.

Florida Medical Association, Hollywood, May 2-4. Dr. Shaler Richardson, 111 West Adams Street, Jacksonville, Secretary.

Georgia, Medical Association of, Macon, May 9-12. Dr. Allen H. Bunce, 139 Forrest Avenue, N. E., Atlanta, Secretary.

Illinois State Medical Society, Peoria, May 16-18. Dr. Harold M. Camp, Lahl Building, Monmouth, Secretary.

Iowa State Medical Society, Des Moines, May 10-12. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Kansas Medical Society, Lawrence, May 2-4. Dr. J. F. Hassig, 804 Huron Building, Kansas City, Secretary.

Massachusetts Medical Society, Boston, June 5-7. Dr. Walter L. Burrage, 182 Walnut Street, Brookline, Secretary.

Medical Library Association, Chicago, June 19-21. Miss Marjorie J. Darrah, 640 Mullett Street, Detroit, Secretary.

Medical Women's National Association, Milwaukee, June 11-12. Dr. Inez A. Bentley, 45 Gramercy Park, New York, Secretary.

Minnesota State Medical Association, Rochester, May 22-24. Dr. E. A. Meyerding, 11 West Summit Avenue, St. Paul, Secretary.

Mississippi State Medical Association, Jackson, May 9-11. Dr. T. M. Dye, Clarksdale, Secretary.

Missouri State Medical Association, Kansas City, May 1-4. Dr. E. J. Goodwin, 634 North Grand Boulevard, St. Louis, Secretary.

Nebraska State Medical Association, Omaha, May 23-25. Dr. R. B. Adams, Center McKinley Building, Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 16-17. Dr. D. E. Sullivan, 7 North State Street, Concord, Secretary.
New Jersey, Medical Society of, Atlantic City, June 6-9. Dr. J. B. Morrison, 66 Milford Avenue, Newark, Secretary.
Oklahoma State Medical Association, Oklahoma City, May 15-17. Dr. C. A. Thompson, Commercial National Bank Building, Muskogee, Secretary.
Rhode Island Medical Society, Providence, June 3. Dr. J. W. Leech, 167 Angell Street, Providence, Secretary.
Society for the Study of Asthma and Allied Conditions, Washington, D. C., May 6. Dr. W. C. Spain, 116 East 53d Street, New York, Secretary.
South Dakota State Medical Association, Huron, May 15-17. Dr. John F. D. Cook, Langford, Secretary.
Texas, State Medical Association of, Fort Worth, May 8-11. Dr. Holman Taylor, Medical Arts Building, Fort Worth, Secretary.
West Virginia State Medical Association, Charleston, May 22-24. Mr. Joe W. Savage, Professional Building, Charleston, Executive Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Issues of periodicals are kept on file for a period of five years only. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending, but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

45: 1-228 (Jan.) 1933

*Intestinal Infections in Infants. Marion M. Johnston, A. Brown, F. F. Tisdall and D. T. Fraser, Toronto, Canada.—p. 1.
Raw Apple Diet in Treatment of Diarrheal Conditions in Children. T. L. Birnberg, St. Paul.—p. 18.
Asthma in Children: Analysis of Eighty-Four Cases. R. Chobot, New York.—p. 25.
*Chemical Action of Sodium Citrate as Cause of Certain Transfusion Reactions. A. S. Minot, Katharine Dodd and R. Bryan, Nashville, Tenn.—p. 32.
*Urea Clearance in Normal and in Dehydrated Infants: Renal Function in Intestinal Intoxication. L. Schoenthal, Dorothy Lurie and Margaret Kelly, New York.—p. 41.
Enteral Administration of Scarlatinal Filtrate Toxin. Jean V. Cooke, St. Louis.—p. 54.
*Results Obtained from Use of Various Tuberculin Tests. E. Friedman, M. H. Black and A. L. Esserman, Denver.—p. 58.
Efficiency of New Orleans Sunshine in Preventing Rickets in Rats. H. Laurens and H. S. Mayerson, New Orleans.—p. 66.
Effect of Sunshine Through Window Glass and Fresh Air on Resistance to Infection: Experiments on Animals. J. R. Ross, Elizabeth Chant Robertson and F. F. Tisdall, Toronto, Canada.—p. 81.
Effects of Cod Liver Oil-Skimmed Milk Feeding on Bones of Infants. H. E. Irish, Chicago.—p. 96.

Intestinal Infections in Infants.—To test the validity of the various hypotheses as to the cause of acute intestinal intoxication, Johnston and her associates subjected 172 infants with acute intestinal intoxication or related diagnosis and 107 controls to a clinical investigation as well as a bacteriologic survey of the flora of the upper respiratory and gastro-intestinal tracts. Although evidence of late involvement of the middle ear developed in 63 per cent of the patients, there was similar involvement in more than 60 per cent of the controls who showed no evidence of acute intestinal intoxication. Hemolytic streptococci were rarely isolated from the ear, nose and throat in the patients either during life or post mortem. Hemolytic streptococci were isolated more frequently from controls both during life and post mortem, although these showed no symptoms suggestive of acute intestinal intoxication. Evidence was found bacteriologically or serologically of infection with pathogenic micro-organisms of the colon-paratyphoid-dysentery group. The authors conclude that acute intestinal intoxication is not caused by masked mastoid infection. Acute intestinal intoxication, fermentative diarrhea, infectious diarrhea, dysentery and summer diarrhea are synonyms indicating one condition—a gastro-intestinal infection with species of the colon-paratyphoid-dysentery group of bacilli.

Chemical Action of Sodium Citrate.—According to Minot and his associates, infants with certain chemical abnormalities of the blood may be harmed rather than benefited by transfusions of citrated blood even when no incompatibility or allergy can be demonstrated. Considerable evidence that the introduction of sodium citrate is the cause of the trouble has been obtained from experiments on animals. Unfavorable reactions have been produced in dogs with low values for blood calcium, with increased guanidine in the blood and with alkalosis by the introduction of an ordinary citrated transfusion or of similar amounts of sodium citrate in saline solution. Though no symptoms of reaction were produced by the injection of equal amounts into normal control animals, the same effect could be produced by much larger doses of citrate. The reaction is typical of an acute lack of calcium and is relieved or prevented by the administration of calcium salts. The results indicate the importance of readjustment of abnormal chemical conditions of the blood before giving citrate transfusions. The authors present the case of an infant in which death followed the transfusion of citrated blood.

Urea Clearance in Infants.—Schoenthal and his associates observed that the urea clearance of nine normal infants corrected for surface area agreed with the values observed by van Slyke and his co-workers and Addis and his collaborators for older children and adults. This would indicate that renal function measured by the ability to excrete urea is as well developed in infants as in later life. In infants suffering from severe diarrhea and vomiting (intestinal intoxication), the urea clearance is often greatly reduced. In the absence of pathologico-anatomic lesions of the kidneys, dehydration and its concomitant effects on body fluids and renal tissue are considered to be the most important factors leading to a reduced urea clearance. The authors conclude that similar observations could be made in other diseases in which dehydration is a prominent symptom. In pyloric stenosis, intestinal obstruction, acute and chronic nephritis, so-called pyelitis and diabetes mellitus, dehydration and oliguria often are pronounced, and an increase in nonprotein and urea nitrogen is frequently observed. It is possible that in these conditions, which are characterized by excessive loss of water from the body (prerenal deviation), the urea clearance may be diminished, and the mechanism of decreased renal function may be analogous to that present in intestinal intoxication.

Results from Various Tuberculin Tests.—Friedman and his associates subjected fifty-five children, chiefly of the preventorium type, with a generous admixture of active bone and pulmonary disturbances, ranging in age from 4 to 17 years and equally divided between the sexes, within a relatively short period to the application of the Mantoux, "single puncture," Pirquet, "multiple puncture" and percutaneous tests. Their study of the various diagnostic tuberculin cutaneous tests, performed with scrupulous regard for details, demonstrated the utter unreliability of the Pirquet and the modified Moro tests. It failed to substantiate the claims advanced by other observers for the "multiple puncture" method. Their study, in their opinion, demonstrated the superiority of the Mantoux and "single puncture" technic. The recommendation appears warranted that these two tests supersede the others. They conclude that for routine office and bedside work the "single puncture method" may be given precedence, because it is easier to perform, is less time consuming, eliminates the necessity for dilution and refrigeration, is less expensive and, withal, yields results as accurate as those obtained by the well established Mantoux test.

American Journal of Hygiene, Baltimore

17: 1-296 (Jan.) 1933

Study of Malarial Relapses in United States Army. W. B. Borden, Washington, D. C.—p. 1.
Controlled Technic for Employment of Naturally Induced Malaria in Therapy of Paresis. M. F. Boyd, Tallahassee, Fla., and W. K. Stratman-Thomas, Jacksonville, Fla.—p. 37.
Studies on Benign Tertian Malaria: I. On Occurrence of Acquired Tolerance to Plasmodium Vivax. M. F. Boyd, Tallahassee, Fla., and W. K. Stratman-Thomas, Jacksonville, Fla.—p. 55.
Effects of Vitamins A and D on Antibody Production and Resistance to Infection. Meridian Ruth Greene, Baltimore.—p. 60.
Comparative Study of Antipneumococcus Serum Containing Heterophile Antibody. H. M. Powell, W. A. Jamieson, G. H. Bailey and R. R. Hyde, Baltimore.—p. 102.
Acute Minor Respiratory Diseases Prevailing in Group of Families Residing in Baltimore, Md., 1928-1930: Prevalence, Distribution and Clinical Description of Observed Cases. V. A. Van Volkenburgh and W. H. Frost, Baltimore.—p. 122.
Cytotropic Viruses, with References to Filtrable Forms of Bacteria and Cancer. E. W. Goodpasture, Nashville, Tenn.—p. 154.

Quantitative Experimental Studies on Rat Nematode Heterakis Spumosa Schneider, 1866. G. F. Winfield, Baltimore.—p. 168.
*Bacteriologic Studies of Milk-Borne Outbreak of Scarlet Fever. H. Welch and F. L. Mickle, Hartford, Conn.—p. 229.
Further Outbreaks of Botulism in Rocky Mountain Region. I. C. Hall, Denver.—p. 235.
Effect of Blood Loss on Resistance of Chickens to Variable Degrees of Parasitism. D. A. Porter and J. E. Ackert, Manhattan, Kan.—p. 252.
Studies on Ichthyophonus Hoferi, Parasitic Fungus of Herring, Clupea Harengus: I. Parasite as It Is Found in Herring. G. E. Daniel, Baltimore.—p. 262.
Rôle of Lipoids in Forssman Antigens. M. Armangué, P. Gonzalez and Sara Romero, Barcelona, Spain.—p. 277.
*Heptylresorcinol in Treatment of Hookworm Infection. N. A. David and H. G. Johnstone, San Francisco.—p. 287.

Milk-Borne Outbreak of Scarlet Fever.—In February, 1932, there occurred near Hartford, Conn., an outbreak of scarlet fever and septic sore throat. The epidemiologic evidence indicated that it was milk borne and accordingly Welch and Mickle made bacteriologic studies of the patients and of the herd apparently involved. Organisms isolated from these patients with scarlet fever and sore throat were found to give the characteristics of Streptococcus scarlatinae. This classification was subsequently confirmed by serologic studies in another laboratory. Two milk handlers, operating a dairy connected with the outbreak by epidemiologic data, harbored in their throats organisms identical in every respect with those isolated from the clinical cases. The authors' studies indicate that the presence of a distinct capsule on a beta hemolytic streptococcus is not sufficient evidence that the organism is Streptococcus epidemicus without further studies on its cultural, biochemical and serologic properties. They also present experimental evidence which indicates that the classification of streptococci on the basis of the type of lesion produced in the animal body is a questionable procedure. It is probable that the course of the infection is subject, in addition to the type of organism involved, to one or both of the following determining factors: 1. Fluctuation or variation in the virulence of different cultures of the same organism. 2. Variation in the individual resistances of the experimental animals, whether due to environmental or to hereditary causes.

Heptylresorcinol in Treatment of Hookworm.—David and Johnstone review the literature and present thirteen cases of hookworm infestation treated with heptylresorcinol. Of these, the six patients who were previously treated over a considerable period of time with olive oil solutions of the drug were unaffected; of the seven receiving the crystalline drug in plain gelatin capsules, two were cleared. Of the ten patients who later received phenyl salicylate coated capsules of the drug, eight were cured. One case of ascariasis was cured by heptylresorcinol in olive oil, but one case of trichuris infestation did not respond to a single treatment of heptylresorcinol in capsules coated with phenyl salicylate. The authors conclude that better results seem to be obtained when precautions are taken to delay or prevent the absorption of heptylresorcinol. Although only a few of their cases compare with Brown's study on the effectiveness of hexylresorcinol in hookworm infestation, the observations indicate that heptylresorcinol is not as satisfactory as hexylresorcinol for hookworm infestation.

American Review of Tuberculosis, New York

27: 1-120 (Jan.) 1933

Fixity of Attenuation of B C G. A. Calmette, Paris, France.—p. 1.
Protection Against Tuberculosis with B C G in Guinea-Pigs. K. E. Birkhaug, Rochester, N. Y.—p. 6.
Tuberculosis and Leukemia. R. H. Jaffé, Chicago.—p. 32.
Benign Pulmonary Tuberculosis with Diabetes. H. Wessler and H. Hennell, New York.—p. 47.
Congenital Cystic Disease of Lung. W. C. Pollock and H. P. Marvin, Denver.—p. 59.
*Spontaneous Pneumothorax with Acute Abdominal Symptoms: Report of Case. W. R. Oechsli and Jane Skillen, Olive View, Calif.—p. 67.
*Fluoroscopy in Tuberculosis Case Finding. H. W. Hetherington and E. W. Flahiff, Philadelphia.—p. 71.
The Tuberculosis Trained Nurse. J. Walsh, White Haven, Pa.—p. 81.
*Costa and Red Cell Sedimentation Reactions in Laryngeal Tuberculosis: Comparative Study. C. L. Rubenstein, Duarte, Calif.—p. 92.
*Protest Against Current Conception of Activity in Pulmonary Tuberculosis. L. H. Fales, Livermore, Calif.—p. 101.

Spontaneous Pneumothorax.—Oechsli and Skillen present a case of spontaneous pneumothorax, in a woman, aged 25, which constitutes one of the more uncommon exceptions to the rule, in that the predominating symptoms were gastro-intestinal (abdominal pain, nausea and vomiting), and dyspnea was practically absent. The authors feel that this variation from the usual symptom complex is probably explained by the fact that the direction of greatest displacement of viscera was downward, with consequent embarrassment of the diaphragm. The heart and mediastinum were moderately displaced, but apparently not sufficiently to cause dyspnea.

Fluoroscopy in Tuberculosis.—Hetherington and Flahiff compare the results of the examination of 347 young adults with the fluoroscope and with stereoscopic roentgenograms. They observed that the fluoroscope fails to reveal a considerable part of the calcified nodules of lungs and lymph nodes visible in roentgenograms. Tuberculous infiltration limited to the apex of the lung above the clavicle is seldom recognizable by fluoroscopic examination. Apical infiltration extending below the clavicle is usually recognizable with the fluoroscope but may be overlooked. The fluoroscope may be used to detect the more extensive and therefore probably the more significant pulmonary lesions, but when fluoroscopic examination does not reveal any pulmonary abnormality the possibility of a significant tuberculous lesion cannot be excluded. Fluoroscopy affords a relatively inexpensive method of selecting children who on further examination will be found to need treatment or prophylactic care for tuberculosis. Lesions suspected with the fluoroscope should always be confirmed by roentgenograms.

Costa and Red Cell Sedimentation Reactions.—An evaluation of the Costa reaction, as modified by Schwartz and the author, and a comparison with the red cell sedimentation reaction are presented by Rubenstein. The material he used for his study was seventy-five cases of pulmonary tuberculosis complicated by laryngeal tuberculosis. He points out that, before instituting any radical form of treatment, it is highly important that the phthisiolaryngologist secure accurate data regarding the patient's pulmonary process and his immunobiologic status. The author recommends the Costa reaction as a determinant of pulmonary activity, in addition to the sedimentation reaction. The Costa and sedimentation reactions disclosed a complete parallelism in cases of far advanced disease. In latent cases and those with moderately advanced disease there was a disparity between the two reactions that favored the Costa reaction in sensitivity. Both reactions were found to be of value in differential diagnosis between simple and tuberculous laryngitis. Tuberculosis of the larynx widens the indications for chest surgery, which, when applied at the proper immunobiologic phase, is a most powerful weapon in effecting a complete cure of laryngeal tuberculosis. It is his opinion that the Costa reaction may be employed profitably in the laryngeal tuberculosis clinic as an objective method for decision as to activity, and as a guide in the treatment to be employed.

Activity in Pulmonary Tuberculosis.—According to Fales, the idea as to what constitutes activity in pulmonary tuberculosis has not kept pace with other advances in knowledge. Although the presence of constitutional symptoms may be considered a manifestation of activity, one must not conclude that the absence of constitutional symptoms means no activity. The old conception, therefore, that activity is determined by the presence of constitutional symptoms, should be discarded as unreliable. The most exact method at one's disposal is to consider activity in terms of the anatomopathologic changes that occur in the lungs. In certain types of tuberculosis, of which the childhood and the secondary tuberculosis of adults are examples, early diagnosis can be made only by the roentgen ray, as physical observations are usually absent and constitutional symptoms, if present, are so slight that they are usually overlooked. It follows that groups of signs and symptoms as diagnostic criteria for the diagnosis of active pulmonary tuberculosis, although a step in advance at the time, have greatly lost their usefulness. If such groups of criteria are to be used in the future, the roentgen ray must receive the place of prominence in such a scheme. In short, positive roentgenograms unaccompanied by other criteria must be considered of sufficient evidence to diagnose active pulmonary tuberculosis. Comparison of serial roentgenograms taken at certain specified intervals should be considered the method of precision in determining activity in pulmonary tuberculosis. Cases should be deemed active as long as comparative roentgenograms show progression or retrogression of the pathologic lesion, and arrested only after a lesion has remained stable for months under capable roentgenographic control.

Annals of Surgery, Philadelphia

96: 801-960 (Nov.) 1932

*Splenectomy in Purpura Hemorrhagica. E. L. Eliason and L. K. Ferguson, Philadelphia.—p. 801.
Tumors of Sternum: Report of Removal of Large Mediastinal Sternal Chondromyxoma. G. J. Heuer, Cincinnati.—p. 830.
Surgical Treatment of Mediastinal Tumors: Removal of Cystic Azygos Lobe from Posterior Mediastinum. S. W. Harrington, Rochester, Minn.—p. 843.
Cancer Problem in General Hospital. H. L. Foss, Danville, Pa.—p. 857.
Temporary Bilateral Abductor Paralysis Without Nerve Injury and Tetany Following Thyroidectomy. H. A. Bruce, Toronto, Canada.—p. 864.
Results Obtained in Treatment of Raynaud's Disease by Sympathetic Neurectomy and in Thrombo-Angiitis Obliterans by Desensitization of Peripheral Sensory Nerves. A. W. Allen, Boston.—p. 867.
*Results of Operative Treatment of Cancer of Breast. F. S. Mathews, New York.—p. 871.
When Should Irradiation with Radium or Roentgen Ray Precede Operation or Be Employed Without Operation? J. C. Bloodgood, Baltimore.—p. 882.
Inoperable and Malignant Tumors. W. Meyer, New York.—p. 891.
Ulceration of Aberrant Gastric Mucosa in Meckel's Diverticulum: Source of Intestinal Hemorrhage. J. M. Mason and G. S. Graham, Birmingham, Ala.—p. 893.
Clinical Aspects and Treatment of Primary Lymphosarcoma of Stomach and Intestines. D. Cheever, Boston.—p. 911.
*Fate of Obstructed Loop in Intestinal Obstruction Following an Anastomosis Around Obstruction Without Resection. W. L. Estes, Jr., and C. E. Holm, Bethlehem, Pa.—p. 924.
Maggots and Osteomyelitis. W. Martin and W. G. Heeks, New York.—p. 930.
Fracture of Neck of Femur: Clinical Criteria in Prognosis. K. Speed, Chicago.—p. 951.

Splenectomy in Purpura Hemorrhagica.—In order to have some basis on which to judge the results and dangers of splenectomy in purpura hemorrhagica, Eliason and Ferguson collected and analyzed the 208 cases reported in the literature and add five unreported cases of their own. A review of the literature points to the fact that purpura hemorrhagica is a disease causing not only a reduction of blood platelets but also a disturbance of the entire reticulo-endothelial system. It has not yet been proved that the spleen is the organ at fault in purpura hemorrhagica. A definitely established diagnosis must be made before splenectomy should be considered. Once the diagnosis is established, the therapeutic indications appear to be (1) the control of the hemorrhage and (2) the removal of the etiologic factors. Splenectomy appears to be the most effective method of controlling extensive hemorrhage in purpura hemorrhagica of either the acute or the recurring type. Early operation and adequate preparation of the patient by transfusion is imperative. Removal of foci of infection is the best prophylaxis against recurrences. The operative mortality for the whole group was 13.1 per cent, but for the cases reported in the last four years the mortality was 7.08 per cent in 113 cases. In acute purpura there were thirty-five cases treated by splenectomy with twelve deaths, 34.3 per cent. In the last twenty-two cases there were only three deaths, 13.6 per cent. In the chronic purpuras there were 160 cases with eleven deaths, 7 per cent. In eighteen of the twenty-eight cases the cause of death appeared to be postoperative shock in a poor risk patient; less frequently, intracranial hemorrhage, operative accidents or postoperative complications, or incorrect diagnoses.

Results of Operative Treatment of Cancer of Breast.—Mathews presents a series of 218 unselected cases of carcinoma of the breast that have been submitted to operation. In 67 per cent the axillary nodes were involved. In thirteen patients the operation is recorded as incomplete, and in several others supraclavicular glands were involved. Of the patients operated on over ten years ago 23.9 per cent survived the ten-year period, and some of these are now living from ten to nineteen years from the date of operation. In a series of patients, which includes a number not usually classed as operable, 37.8 per cent have passed the five-year period. The results compare favorably with those of well known operating surgeons and seem as good as the results of those who largely replace surgery by irradiation. The author has no intention to replace operative surgery in operable cases by any form of radiation but hopes to continue the operative treatment with as much aid from radiation as the methods now in use or to be developed may offer.

Obstructed Loop in Intestinal Obstruction.—Estes and Holm state that, following an entero-anastomosis around a mass of intestinal adhesions, uneventful recovery is to be anticipated unless intestinal obstruction in the adherent coils persists or recurs. If the obstruction persists or recurs there will follow an ulcerative enteritis and dilatation of the obstructed loops, which may lead to a general enterocolitis evidenced by diarrhea, visible peristalsis and borborygmus. Resection of the side-tracked ulcerated intestine will be necessary. Entero-anastomosis for intestinal obstruction must be looked on as a possible first stage operation of which resection of the obstructed loops may be required as a second stage. No matter whether the anastomosis is an ileo-ileostomy or an ileocolostomy, in the presence of obstruction the ulceration will occur. That the obstruction and subsequent stagnation play the major part in the cause of the ulceration seems proved by the fact that clinically and experimentally in a blind loop of intestine left distal to an anastomosis a similar ulceration will be produced; in other words, if the obstruction in the sidetracked intestine remains, it acts like a blind loop left distal to a lateral anastomosis. In the presence of acute obstruction it would be unwise to consider primary resection of the obstructing coils unless gangrenous, but if at the time of lateral anastomosis it is certain that the obstruction in the adherent area remains, the two stage operation must be definitely planned.

Archives of Internal Medicine, Chicago

51: 1-172 (Jan.) 1933

Syndrome of Anemia, Glossitis and Dysphagia: Report of Eight Cases, with Especial Reference to Observations at Autopsy in One Instance. M. M. Suzman, London, England.—p. 1.
*Blood Cholesterol in Thyroid Disease: I. Analysis of Findings in Toxic and Nontoxic Goiter Before Treatment. L. M. Hurxthal, Boston.—p. 22.
*Intravenous Pressure: I. New Method of Determination. W. A. Brams, L. N. Katz and W. J. Schutz, Chicago.—p. 33.
Transient Methemoglobinemia Due to Ammonium Nitrate. L. Tarr, New York.—p. 38.
Endemic Nutritional Edema: II. Serum Proteins and Nitrogen Balance. J. B. Youmans, A. Bell, Dorothy Donley and Helen Frank, Nashville, Tenn.—p. 45.
*Detection of Murmur of Acute Pericarditis: Description of New Clinical Procedure. H. N. Segall, Montreal, Canada.—p. 62.
*Acute Leukemia Following Lymphosarcoma. K. Kato and A. Brunschwig, Chicago.—p. 77.
Toxicity of Purified Bile Preparations: III. Influence on Cardiovascular Responses. F. A. Ries and E. U. Still, Baltimore.—p. 90.
Splenectomy in Sickle Cell Anemia: Report of Case with Necropsy in Adult on Whom Splenectomy Was Attempted. R. E. Ching and L. W. Diggs, Memphis, Tenn.—p. 100.
Nourishment of Myocardium Through Thebesian Vessels in a Heart in Which the Large Coronary Arteries and Veins Were Destroyed by Tuberculous Myocarditis. S. Bellet, B. A. Gouley and T. M. McMillan, Philadelphia.—p. 112.
*Treatment of Elderly Diabetic Patients with Cardiovascular Disease: Available Carbohydrate and Blood Sugar Level. S. Soskin, L. N. Katz, S. Strouse and S. H. Rubinfeld, Chicago.—p. 122.
*Yellow Atrophy of Liver: Report of Case, with Particular Reference to Metabolism of Copper. A. H. Gordon and I. M. Rabinowitch, Montreal, Canada.—p. 143.
Distention as Factor in Intestinal Obstruction. R. C. Herrin and W. J. Meek, Madison, Wis.—p. 152.

Blood Cholesterol in Thyroid Disease.—Hurxthal determined the blood cholesterol during fasting as a routine in 505 patients with thyroid disease, along with the pulse, the weight and the basal metabolic rate. He observed that the lowest average values for blood cholesterol were in patients in or near thyroid crises. Auricular fibrillation in toxic goiter was associated with the next lowest average level of cholesterol. The average cholesterol value in all types of exophthalmic goiter was lower than in toxic adenomatous goiter. Recurrent hyperthyroidism was associated with cholesterol values that were almost as low as those in exophthalmic goiter. The average cholesterol value in nontoxic goiter was normal, although the scatter was wider than the author expected. Age appeared to raise the blood cholesterol in these cases. Chronic thyroiditis was associated with higher average values than in any other thyroid disease except myxedema. The level of the blood cholesterol and the basal metabolic rate bore a reciprocal relationship when judged by average values.

Intravenous Pressure.—Brams and his associates' method of estimating the intravenous pressure is based on the principle that the superficial veins on the dorsum of the hand can be easily visualized in a darkened room by placing a small light, such as an ordinary pocket flashlight, against the palmar surface, preferably in the interosseous spaces. The superficial veins by this transillumination appear as black bands, which can be obliterated by moderate pressure and thus distinguished from shadows cast by ligaments. After the patient has been

placed at rest for ten minutes in a horizontal or semirecumbent position, the arm and hand to be examined are supported horizontally by a pillow and held at a level which corresponds to the point of entrance of the vena cava into the right auricle. The mouth of a small glass funnel is covered by a thin rubber dam held securely in place by a thread tied tightly in a previously prepared groove near the rim. A small hole is then cut in the center of the rubber dam, through which the vein to be examined is visualized. The surface of the rubber dam is then covered with rubber cement, and the funnel is placed on the dorsum of the hand so that the previously selected vein is seen through the aperture in the rubber. The funnel is held in place by moderate pressure until the rubber is adherent to the skin. The tip of the funnel is then connected by rubber tubing to a suitable water manometer, which is so graduated that pressure may be read in millimeters of water. The room is darkened, or a black cloth is placed over the head of the observer, and the light is placed against the palmar surface of the hand in order to visualize the dorsal vein within the aperture of the rubber dam. The air pressure is then slowly raised in the instrument by a suitable rubber bulb—with the leak-valve shut—until the vein under examination becomes obliterated as a result of the external compression. It is important to distinguish two stages; the first is the obliteration of the vein, and the second, further blanching of the skin. The authors selected the former as the end-point at which the pressure is read off in the manometer in millimeters of water. They examined a series of twelve patients and later compared the results with those obtained by the direct method. They observed that a high degree of accuracy is possible with their indirect method. They believe that with minor improvements the method can be adopted for general clinical use.

Detection of Murmur of Acute Pericarditis.—Segall states that the pericardial friction murmur is a clinical sign, the detection of which depends on methods of eliciting it and of differentiating it from other murmurs that may be heard over the precordium. From the point of view of the observer in search of clinical signs, the discovery of a typical leathery friction rub in the course of an ordinary examination of the heart may be looked on as a fortunate accident. Respiratory movements, postural changes and shaking or rolling of the body may cause a pericardial friction murmur to appear, to vanish and to reappear, and they may alter the loudness, quality and position of the murmur. These procedures, therefore, constitute methods of eliciting a friction murmur and of differentiating it from other murmurs which it may resemble.

Leukemia After Lymphosarcoma.—Kato and Brunschwig review the literature and report in detail two cases in which acute leukemia followed roentgen treatment for lymphosarcoma. When the patients were first seen they presented a normal blood picture; a short time later, acute lymphatic leukemia developed with a rapidly fatal termination. The authors believe that this is additional evidence in favor of the view that lymphosarcoma and lymphatic leukemia are only different stages in the same pathologic process. As they instituted roentgen therapy in both of their cases immediately after they made a diagnosis of lymphosarcoma, the question arises as to whether or not this treatment induced the leukemic state.

Treatment of Elderly Diabetic Patients with Cardiovascular Disease.—Soskin and his associates confirm the characteristic myocardial impairment resulting from insulin hypoglycemia reported by other workers. Their results indicate that the changes in the ST segment and T wave of the electrocardiogram following the administration of insulin depend on the direction of the major deflection of the QRS complex, a correlation heretofore overlooked. They obtained similar results by the therapeutic use of insulin, in amounts that did not cause hypoglycemia, in the treatment of elderly diabetic patients with cardiovascular disease. The results that they obtained with insulin they also obtained by the use of a low carbohydrate diet without insulin. The objective manifestations of myocardial impairment obtained with both insulin and a low carbohydrate diet were almost always accompanied by complaints of subjective distress in their patients. They conclude that the deleterious action of insulin on the heart is probably not due to a direct toxic action on the myocardium but is probably related to the supply of carbohydrate that is readily available to this organ.

Yellow Atrophy of Liver.—The literature on the metabolism of copper is briefly reviewed by Gordon and Rabinowitch, and, though the data are not conclusive, they do suggest that copper, a normal constituent of food, may be harmful when administered in excess quantities. They report a case of acute yellow atrophy of the liver in which the liver was found to contain an enormous amount of copper. In spite of the large amount of copper, there was no arsenic. Though it may be difficult to associate the anatomic changes in the liver with the exposure of the patient to copper as long as fifteen years ago, there is a reasonable chemical basis for this association. There is, first, the incontestable fact that the liver contained a large amount of copper—as far as they could ascertain, the largest amount on record. They suggest that the failure of the liver to excrete the copper may have been due to the fact that copper forms with protein a series of quite stable proteinates. The liver is also rich in products of protein digestion, many of which also form with copper quite stable compounds. This fact is frequently made use of in quantitative analysis. They conclude that the purpose of reporting their case is to prompt further investigation, in view of the present widespread and increasing use of copper therapeutically. Though copper may have its use, its too general use might do harm. It suggests an analogy in the experiences with the incorporation of iodine in table salt for the prevention of goiter.

Archives of Pathology, Chicago

15: 1-174 (Jan.) 1933

Fate of Endometrial Emboli in Venous Circulation of Rabbit. V. C. Jacobsen, Albany, N. Y.—p. 1.
Fenestrated Hammock-Like Structure in Left Cardiac Atrium: Review of Literature and Report of Case. F. C. Helwig, Kansas City, Mo. —p. 8.
Bone Lesions in Rats Produced by Substitution of Beryllium for Calcium in Diet. S. A. Jacobson, New York.—p. 18.
*Histologic Changes in Rabbits and in Dogs Following Intravenous Injection of Thorium Preparations. E. Shute and M. E. Davis, Chicago. —p. 27.
*Necrotizing Arteritis and Subacute Glomerulonephritis in Gonococcic Endocarditis: Toxic Origin of Periarteritis Nodosa. M. Helpern and M. Trubek, New York.—p. 35.
Persistent Truncus Arteriosus and Congenital Absence of One Kidney with Other Developmental Defects. D. C. Beaver, Rochester, Minn. —p. 51.
*Manual Strangulation. T. A. Gonzales, New York.—p. 55.
Comparison of Hypertrophic Changes in Thyroid Caused in Different Species by Acid Extract of Anterior Lobe of Bovine Pituitary Gland. E. W. Thurston, St. Louis.—p. 67.
*Primary Epithelial Tumors of Vermiform Appendix: Observations by Silver Impregnation. G. Van S. Smith, Brookline, Mass.—p. 78.

Histologic Changes Following Injection of Thorium Preparations.—By means of intravenous injections of thorotrast and similar thorium preparations, Shute and Davis secured the visualization of the spleen and liver in rabbits and dogs, but they were unable to visualize the placenta. They used smaller relative doses than other authors did for successful placental visualization in the rat. These doses, however, produced intense degeneration, particularly of the liver and spleen, caused one of their rabbits to abort, and produced spontaneous rupture of the spleen as well as a fatal postpartum hemorrhage. Particles of thorotrast practically disappear from the liver and spleen in from two to three months after their injection, and the cells by that time regain almost a normal appearance. The placenta of the dog and of the rabbit appears to be an effective barrier to the transmission of thorium to the fetus. With the one exception, all their pregnant animals carried their young to term or were killed near term for purposes of study. The metal could be found in the rabbit placenta microscopically up to eleven days after injection, but by this time it was in the form of fine particles and after that seemed to disappear. They were unable to stain the thorium particles in the tissues. The placental cells did not show the destructive changes seen in the cells of the liver and spleen.

Necrotizing Arteritis and Glomerulonephritis in Endocarditis.—In a case of subacute glomerulonephritis of ten weeks' duration, death occurred from uremia with pericarditis. The onset of this illness occurred eight weeks after a gonococcic urethritis complicated by a gonococcic ophthalmia. At necropsy, Helpern and Trubek found a right-sided subacute gonococcic endocarditis of the pulmonic valve and a typical subacute glomerulonephritis. In addition, isolated necrotizing inflammatory lesions of the small arteries were found in two widely separated regions of the body: the choroid coat of the

eye and the testis. These vascular lesions exhibited many of the morphologic features described in periarteritis nodosa and were considered as belonging to that group. The larger arteries of the body were not involved, and the distribution of the lesions was not extensive enough to produce clinical manifestations. The renal lesion represented a severe reaction of a sensitive organ to the toxin produced by the gonococci growing on the pulmonic valve. The vascular lesions, which in their case were anatomically dissociated from the kidney, were also considered a specific reaction of sensitive vessels to this toxin. Their observations strengthen the conception that these vascular lesions and those of periarteritis nodosa do not represent a specific disease but rather a specific reaction of the blood vessels to any of a whole group of variable toxins.

Manual Strangulation.—Gonzales studied twenty-four cases of manual strangulation with a view to correlating the post-mortem lesions. They represent approximately 0.7 per cent of the total number of homicides, indicating the comparative rarity of this form of violent death. Nearly half of the cases presented injuries of the larynx or of the hyoid bone, and deep hemorrhages were observed in the entire series, contrasting with suicidal hangings, in which complete absence of these lesions was common. The diagnostic significance of the surface lesions, deep cervical hemorrhage and injuries to the thyroid alae, cricoid cartilage and tracheal rings is stressed. No instance of precipitate death from irritation of cervical nerves could be demonstrated, and the difficulty of diagnosis is indicated.

Primary Epithelial Tumors of Vermiform Appendix.—Smith states that the incidence of primary epithelial tumor of the appendix encountered at his clinic is 0.27 per cent. He briefly describes twenty-one carcinoids in relation to clinical and pathologic observations and argentaffin characteristics which link these tumors with the argentaffin cells of the appendix. He describes one primary columnar cell adenocarcinoma of the appendix. It did not reduce silver. Another appendix contained metastatic squamous carcinoma of the cervix which did not reduce silver. He believes that from a study of the argentaffin cells of 261 appendixes the following statements seem justified: Regardless of the age of the patients, the symptoms and the amount of inflammation, the number of argentaffin cells varies considerably. In general, the number of these cells decreases with age and inflammation, especially if symptoms are present.

Iowa State Medical Society Journal, Des Moines

23: 1-58 (Jan.) 1933

Great Importance of Medical Profession in Scheme of National Defense. G. A. Skinner, Omaha.—p. 1.
Comparative Study of Pericarditis. H. L. Smith and F. A. Willius, Rochester, Minn.—p. 6.
Roentgenology as Aid to Obstetric Diagnosis. E. L. Rypins, Iowa City.—p. 12.
Fecal Impaction. C. J. Drueck, Chicago.—p. 14.
Chest Pain Caused by Superficial Thrombophlebitis. E. E. Kottke, Des Moines.—p. 18.
Achlorhydria. Julia Cole, Iowa City.—p. 20.
Quinine Amblyopia or Retrobulbar Neuritis Consequent to Giving of Optochin Base. Grace M. Sawyer, Woodward.—p. 25.

Johns Hopkins Hospital Bulletin, Baltimore

52: 1-117 (Jan.) 1933

*Pathogenesis of Tuberculous Meningitis. A. R. Rich and H. A. McCordock, Baltimore.—p. 5.
Jake Paralysis: Paralysis Following Ingestion of Jamaica Ginger Extract Adulterated with Triorthocresyl Phosphate. J. G. Kidd and O. R. Langworthy, Baltimore.—p. 39.
*Five Cases of Addison's Disease with So-Called Atrophy of Adrenal Cortex. G. L. Duff and C. Bernstein, Baltimore.—p. 67.

Pathogenesis of Tuberculous Meningitis.—Rich and McCordock present experimental and morphologic evidence which demonstrates that diffuse tuberculous meningitis is not a direct and immediate result of hematogenous infection of the meninges. Miliary tuberculosis produces only rare, sparsely scattered tubercles in the meninges, not diffuse meningitis. Tuberculous meningitis has its origin in the discharge of bacilli into the cerebrospinal fluid from adjacent, older caseous tuberculous foci. Such discharging foci have been found, by careful search, in the substance of the brain or cord, in the meninges, in the bones encasing the central nervous system, or in the choroid plexus in seventy-seven of the eighty-two cases of meningitis in their series. In all except two of these seventy-seven cases the demonstrated source of the diffuse meningitis was situated in the substance of the central nervous system or in the meninges. In the five cases in which no local focus was found, the material for study was incomplete.

Addison's Disease with Atrophy of Suprarenal Cortex.—Duff and Bernstein report five cases of Addison's disease, four of which they treated with suprarenal cortex extract. All of them showed more or less complete "atrophy" of the suprarenal cortex. The destructive process in the suprarenals consisted of a progressive necrosis of cortical cells with collapse of the stroma. In two cases there was regeneration of cortical tissue. The medulla was affected to a much less degree, usually showing only a slight increase in the density of the fibrous framework and some shrinkage of the medullary cells. Lymphocytic infiltrations were constantly present in the suprarenal medulla and among the remnants of cortical tissue. Lymphocytic infiltrations in various situations constituted the most constant observations in association with the suprarenal lesions. Marked hyperplasia of lymphoid tissue was not present in any of the cases. No lesions were found for which the treatment with suprarenal cortex extract could be held responsible. The authors discuss the relation of the pathologic observations to the clinical observations. A consideration of the possible factors in the etiology of the suprarenal lesions leads them to the conclusion that a circulating toxin of unknown origin and nature is probably the causative agent. Four of their cases showed early stages of destruction of the suprarenal cortex but presented no clinical evidence of Addison's disease. These observations indicated that the suprarenal lesion is primary in the cortex and that the three zones of the cortex differ in their susceptibility to damage.

Journal of Experimental Medicine, New York

57: 1-180 (Jan. 1) 1933

Studies on Mouse Leukemia: VII. Relation of Cell Death to Potency of Inoculated Cell Suspensions. M. N. Richter and E. C. MacDowell, New York.—p. 1.
Active Immunization of Mice with Polysaccharides of Pneumococci Types I, II and III. J. Zozaya and Janet Clark, Glenolden, Pa.—p. 21.
Immunologic Reactions Between Agar-Agar and Some Bacterial Antiserums. J. Zozaya and L. Medina, Glenolden, Pa.—p. 41.
Observations on Cultivation of Vaccine Virus in Lifeless Mediums. T. M. Rivers and S. M. Ward, New York.—p. 51.
Rôle of Spleen in Iron Metabolism as Elucidated by Changes in Iron Balance After Splenectomy. Elizabeth D. Wilson and E. B. Krumbhaar, Philadelphia.—p. 65.
Studies on Bartonella Muris Anemia: VIII. Changes in Chemical Constituents of Blood During Anemia. Marta Sandberg, D. Perla and Jessie Marmorston-Gottesman, New York.—p. 81.
Immunity Reactions of Human Subjects to Strains of Pneumococci Other than Types I, II and III. M. Finland and W. D. Sutliff, Boston.—p. 95.
Allergic Lobar Pneumonia: Experimental Study. B. M. Fried, Boston.—p. 111.
Occurrence of Antigoitrous Substances in Plants. D. Marine, E. J. Baumann, B. Webster and Anna Cipra, New York.—p. 121.
Study of Therapeutic Mechanism of Antipneumococcic Serum on Experimental Dermal Pneumococcus Infection in Rabbits: II. Comparison of Therapeutic Effect of Unrefined, Antipneumococcic Serum with that of Its Various Protein Fractions: Rôle of Nonantibacterial Factor. A. B. Sabin, New York.—p. 139.
Morphology of Bacterium Shigae Cultivated on Various Mediums Favorable to Development of Filtrability and Life Cycle Forms. R. W. G. Wyckoff, New York.—p. 165.

Kentucky Medical Journal, Bowling Green

31: 1-72 (Jan.) 1933

How Can You as Family Physician Lessen the Frequency and Complications of Grip, Influenza or Flu? R. W. Bledsoe, Covington.—p. 20.
Difficult Fractures. W. B. Owen, Louisville.—p. 27.
Meningococcic Meningitis Treated with Through-and-Through Drainage: Case. J. W. Bruce, Louisville.—p. 31.
Hydrophobia: Case Report. D. S. Robertson, Symsonia.—p. 33.
Some Problems in Pediatrics. J. H. Pritchett, Louisville.—p. 35.
Community Health. H. Linden, Harlan.—p. 37.
Nonsurgical Treatment of Lymphoid Tissue of Throat. E. C. Yates, Lexington.—p. 39.
Prenatal Syphilis. W. U. Rutledge, Louisville.—p. 41.
Reminiscences of Medicine. H. A. Kelly, Baltimore.—p. 44.
Management of Cutaneous Burns in Children. E. C. Davidson, Detroit.—p. 46.
Ethylene Anesthesia. H. S. Eggers, Louisville.—p. 51.
Use of Bismuth in Treatment of Syphilis. C. C. Barrett, Lexington.—p. 57.
Treatment of Diarrhea in Infants. T. J. Marshall, Paducah.—p. 60.
Complications of Labor. B. S. Rutherford, Bowling Green.—p. 62.
Treatment of Intestinal Obstruction. G. A. Hendon, Louisville.—p. 65.

Maine Medical Journal, Portland

24: 1-20 (Jan.) 1933

*Transurethral Prostatic Resection: Review of Recent Literature and Personal Observations. C. N. Peters, Portland.—p. 4.
Neurosyphilis: Results of Treatment at Bangor State Hospital. C. J. Hedin, Bangor.—p. 7.

Transurethral Prostatic Resection.—Peters reviews the literature and from its study states that transurethral prostatic resection is a distinct step forward in the urologic field. Its application to many types of bladder neck obstruction is a feasible and practical method of relief. In malignant prostates, it offers the best way of dealing with obstruction to the urinary flow with the least possible hardship to the patient. Its immediate surgical results are gratifying to the patient and reassuring to the physician. It is too recent a procedure to draw conclusions as to end-results or its value in replacing prostatectomy in all cases. It is a major surgical operation for the use of trained specialists accustomed to dealing with pathologic changes of the bladder neck.

Michigan State M. Society Journal, Grand Rapids

32: 1-74 (Jan.) 1933

Work Plan for Section on Gynecology and Obstetrics. N. F. Miller, Ann Arbor.—p. 1.
Tumors and Their Behavior. H. J. Vanden Berg, Grand Rapids.—p. 4.
Bacteriophage. M. H. Soule, Ann Arbor.—p. 8.
*Treatment of Diabetic Coma. W. V. Vander Voort, Battle Creek.—p. 14.
Some Physical and Social Aspects of Malnutrition in School Children. J. G. Slevin, Detroit.—p. 21.
Gynecologic Symptoms of Maladjusted Woman. B. W. Malfroid, Flint.—p. 25.
Injuries of Knee Joint. C. W. Peabody, Detroit.—p. 28.
Sickle Cell Anemia in Six Months Old Colored Female Infant: Report of Case. Hira E. Branch, Detroit.—p. 35.
Michigan Department of Health. C. C. Slemons, Lansing.—p. 36.

Treatment of Diabetic Coma.—Vander Voort believes that diabetic coma is an emergency which demands an immediate, heroic, uninterrupted, and personally supervised treatment. The alveolar carbon dioxide tension estimation is invaluable as a time saver and is a reliable index for the institution of immediate treatment. The basic foods excel in the prevention and treatment of coma. Factors that tend to increase the hydrogen ion concentration of the blood should be carefully searched for and eliminated, if possible. All foci of infection should be removed as quickly as the patient's condition will permit. He believes that in desperate moribund cases the mortality percentage can be greatly reduced by the careful administration of larger quantities of fluid and insulin, the dosage depending on the age of the patient and the condition of the cardiovascular system. The initial and subsequent dosage of insulin is unknown, as every patient is a law unto himself, but enough must be given to control the coma, regardless of the amount used. Coma, if taken in time, usually vanishes before insulin, salt, water and work. As soon as the oral administration of food is tolerated, the patient should be given easily absorbed, nonirritating and well strained liquids in small amounts at not too frequent intervals, fats and proteins being eliminated as nearly as possible, at least for the first twenty-four to forty-eight hours. No patient should be permitted to leave the hospital until he has been instructed in rudimentary diabetic dietetics, urinary analysis, and at least a few symptoms and preliminary treatment of coma and insulin reaction.

New Jersey Medical Society Journal, Orange

30: 1-122 (Jan.) 1933

Simple Method of Pelvimetry by Roentgenography. J. H. Underwood and E. E. Downs, Woodbury.—p. 1.
*Cervical Infections. T. B. Lee, Camden.—p. 2.
Treatment of Eclampsia. S. A. Cosgrove, Jersey City.—p. 6.
Cesarean Section as Positive Factor in Maternal Mortality. J. C. Brown, Atlantic City.—p. 16.
Progress in Prevention and Control of Eclampsia. J. O. Arnold, Philadelphia.—p. 22.
Clinical Anatomy and Physiology of Colon. V. Knapp, Asbury Park.—p. 26.
Preventive Medicine from Standpoint of Internist: Its Value for Public Health. L. F. Barker, Baltimore.—p. 29.

Cervical Infections.—Lee states that young children often suffer with leukorrhea which recurs at times and varies in amount during a period of years. More often than is commonly suspected the cervix is infected. The difficulty encountered, and the patience required, too often result in neglect of these patients. Cervicitis is the chief cause of sterility, and the cause most amenable to treatment. The cervix is potentially infected in every case of labor or abortion. Cervicitis is important as a source of focal infection, so far as the pelvic organs are concerned. Leukorrhea should be regarded as indicating cervicitis until proved otherwise. The close relationship between cervicitis and cancer of the cervix should be always kept in mind. Cervices in which chronic infections have been cured apparently do not develop cancer.

Psychiatric Quarterly, Albany, N. Y.

7: 1-190 (Jan.) 1933

Pilgrim State Hospital. F. W. Parsons, Albany, N. Y.—p. 5.
Review of Work of Psychiatric Institute and Hospital During Past Year. C. O. Cheney, New York.—p. 16.
Family Care and Institution Problem. H. M. Pollock, New York.—p. 28.
Psychoses in Identical Twins: Contribution to Study of Etiology of Functional Psychoses. W. E. Merriman, Poughkeepsie, N. Y.—p. 37.
Present and Future Outlook in Treatment of Amentia. L. P. Clark, New York.—p. 50.
*Tumors of Pituitary Gland and Its Neighboring Structures. L. M. Davidoff, New York.—p. 72.
Nervous System and Antibody Production. N. Kopeloff, L. M. Kopeloff and M. E. Raney, New York.—p. 84.
Investigation of Methods of Measurement of Electrical Phenomena of Skin. C. Landis and T. W. Forbes, New York.—p. 107.
Experimental Toxic Approach to Mental Diseases—Reaction of Brain Tissue to Subcutaneous Injection of Enterogenous Toxic Substances—Indole and Histamine: Part II. A. Ferraro and J. E. Kilman, New York.—p. 115.

Tumors of Pituitary Gland and Its Neighboring Structures.—Davidoff points out that the pituitary gland is a complex organ presiding over the growth of the body, its metabolism and the regulation of function of most of the other endocrine glands. Its position is in close proximity to the vegetative centers of the hypothalamic region, the optic chiasm and the circle of Willis. Tumors of the pituitary and its neighboring structures, while presenting many symptoms in common, vary in their clinical manifestations according to their origin, character, size, position and direction of growth. By means of these variations, most of them can usually be diagnosed clinically. Such accurate diagnoses are important in guiding the plan of treatment. The treatment is generally of a surgical nature, sometimes in combination with roentgen therapy, although at times the latter alone may be used to advantage.

Public Health Reports, Washington, D. C.

47: 2325-2364 (Dec. 23) 1932

Public Health Organization and Administration in Naples, Italy. J. G. Townsend and E. Buonocore.—p. 2328.

47: 2365-2394 (Dec. 30) 1932

Rocky Mountain Spotted Fever (Eastern Type): Virus Recovered from Dog Tick Dermacentor Variabilis Found in Nature. L. F. Badger.—p. 2365.
Endemic Typhus Fever Virus Recovered from Wild Rat Trapped at Typhus Focus in United States. R. E. Dyer, W. G. Workman and A. Rumreich.—p. 2370.

48: 1-26 (Jan. 6) 1933

*Modification of Vaccine Response in Rabbits by Application of Diphtheria Toxin to Vaccination Site. C. Armstrong.—p. 1.
Study of Some Vitamin B Adsorbates. V. Birckner.—p. 7.

48: 27-62 (Jan. 13) 1933

Trends of Health in United States. R. H. Britten.—p. 27.
Influence of Oxygen Tension on Rate of Autolysis of Certain Malignant Tumors and Normal Tissues. Mary E. Maver, J. M. Johnson and C. Voegtlin.—p. 42.

Modification of Vaccine Response.—Armstrong in his experimental studies found that diphtheria toxin when added in suitable amounts to vaccine virus exerts a deterrent local action on the take in rabbits and renders the systemic response less severe. The deterrent action of diphtheria toxin on vaccinia is neutralizable by diphtheria antitoxin. The deterrent action is apparently occasioned by the local cellular reaction rather than by any direct action of the diphtheria toxin on the virus. The site of a positive Schick response in rabbits remains relatively insusceptible to vaccine virus for at least twenty days.

Tennessee State Medical Assn. Journal, Nashville

26: 1-46 (Jan.) 1933

Epiphyseal Separations. A. H. Meyer, Memphis.—p. 1.
Lead Poisoning in Children in Nashville. J. S. Crutcher, Jr., Nashville.—p. 20.
Review of the Organization and Early History of Upper Cumberland Medical Society. W. B. Young, Bon Air.—p. 24.
Failing Heart of Middle Life. W. J. Matthews, Johnson City.—p. 29.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1: 1-46 (Jan. 7) 1933

*Etiologic Factors in Osteo-Arthritis of Hip Joint. R. C. Elmslie.—p. 1.
*Surgical Treatment of Osteo-Arthritis of Hip. E. W. H. Groves.—p. 3.
Sinusitis and Its Radiologic Demonstration. H. K. G. Hodgson.—p. 5.
Adenoma of Islets of Langerhans Associated with Hypoglycemia. R. McD. Cairns and S. E. Tanner.—p. 8.
Pancreatic Cysts. D. Smith.—p. 11.
*Total Avulsion of Scalp: New Method of Restoration. G. F. Mitchell.—p. 13.

Etiologic Factors in Osteo-Arthritis of Hip.—Elmslie classes the etiologic factors concerned in the production of osteo-arthritis of the hip as traumatic, mechanical, toxic, chemical and local disease of the articular ends of the bone. When once the degenerative changes have started, alterations occur in the shape of the bones entering into the articulation, so that whatever the original cause an additional mechanical factor is then induced. These alterations eventually give rise to roentgen appearances that make it difficult to assess how much of the deformity is due to the arthritis and how much was preexistent. There is, however, sufficient evidence of the importance of the mechanical factors in producing osteo-arthritis of the hip to make one always think of the possible late results when one is treating deformity of this joint earlier in life, so that one should always bear in mind that the mechanics of the joint should be kept as nearly natural as possible. Osteo-arthritis of the hip is far more common in men than in women and occurs particularly in manual workers and in athletes. Strain and minor injury must be important factors, but in the majority of patients it is impossible to ascribe the condition to any particular accident. It is not unusual, however, to find that dislocation of the hip or an intracapsular fracture leads after an interval to the development of the characteristic degenerative changes. The various major joints subject to osteo-arthritic changes, the author concludes, are that the upper limb, the shoulder and the wrist are seldom affected, but the elbow frequently undergoes changes in which the joint surfaces are eroded and osteophytes develop, and in the lower limb the hip and knee are most often affected, the ankle seldom.

Surgical Treatment of Osteo-Arthritis of Hip.—Groves states that because osteo-arthritis of the hip is essentially a process of wear and tear, resulting from two main factors—age and trauma—to which some toxic factor may be added in a minor degree, treatment usually is only palliative and not radical or curative. But on the other hand the relief of pain is a great achievement, and he states with considerable conviction that patients with hip osteo-arthritis treated by a well chosen operation are nearly always extremely grateful and satisfied with the measure of relief afforded them. Operative treatment is especially indicated in monarticular arthritis of comparatively young patients and in cases in which trauma has been a causative factor and pain a prominent result. Under these conditions he feels confident that operation can afford relief in all cases, but it requires judgment and a chastened experience to choose the right type of operation for each case. Apart from small variations in the pathologic changes, there are two widely different types of osteo-arthritic hips. In one, the socket is shallow and inadequate, and there seems to be almost a subluxation, so little does the femoral head fit into the acetabulum. Such cases are often old Perthes disease or the result of congenital dislocation that has been reduced. In the other, the socket is deep and the head large. There is so much osteophytic growth round the articular margin of the head that the neck of the femur is nearly as thick as the head. The author concludes that cheilotomy is indicated in marked osteophytic outgrowths resulting from trauma and confined to one hip; modified arthroplasty in the hip in which the socket is deep, the head and neck enlarged so that the joint has become "seized," either lessening the head or removing part of the socket; arthrodesis in the painful hip; excision on the worst side in double arthritis with stiffness of both hips and much pain; and osteotomy in cases with varus deformity or subluxation osteotomy.

Total Avulsion of Scalp.—Mitchell reports a case of total avulsion of the scalp in which he adopted the following method of restoration: The denuded area and the remaining shaved scalp were dressed in saline packs. Under full anesthesia a series of incisions extending down to the pericranium were made, three on the lateral and two on the anterior and posterior aspects, the resulting flaps being three-fourths inch wide and care being taken to leave sufficient attachment at each end of the flaps to allow an adequate blood supply. No attention was paid to hemorrhage, and each succeeding whole-thickness flap was undercut and levered toward the center. The upper lateral flaps were first sutured together with strong catgut; the next lateral flaps were then sutured to the first, leaving a gap of half an inch, and then the third lateral flaps were sutured to the second, leaving another gap of half an inch. The anterior and posterior flaps were treated in the same manner. During this time the hemorrhage was easily controlled by pressure. The whole operation area was then flushed with a 0.5 per cent solution of chlorine. A large sheet of oiled silk soaked in petrolatum was spread over it, subsequent pressure being obtained by means of a capeline bandage. At the end of a week in the author's case the flaps were firmly adherent to the pericranium. Three weeks after the operation the center gaps were rather wider than anticipated, but the granulations were healthy. Under full anesthesia the author made two tongue flaps from the back of the scalp and turned them up into the adjacent gaps, after having removed the thick granulations. None of the hair-bearing scalp flaps were destroyed, and four months later the hair was growing well, the granulation areas being smooth and flush with the adjacent scalp. The bandages were removed at this time, as the patient was receiving mild doses of ultraviolet radiation every second day. The author concludes that the actual operation takes little time and the narrow channels between the flaps require no attention, the granulations filling the gaps completely. The postoperative appearance is a source of satisfaction, because there is hair on the top of the head.

East African Medical Journal, Nairobi

9: 275-307 (Jan.) 1933

The White Man in East Africa. D. V. Latham.—p. 276.
Yellow Fever Problem as It Affects Tanganyika Territory, Together with Notes on Recent Literature on Yellow Fever. R. R. Scott.—p. 283.
Clinical Study of Pneumonia Among Africans. H. C. Trowell.—p. 294.
Transposition of Viscera: Case. J. A. Carman.—p. 305.

Journal of Physiology, London

77: 111-206 (Jan. 16) 1933

Heat Production of Crustacean Nerve. Mary Beresina and T. P. Feng.—p. 111.
Localization of Action of Drugs on Pulmonary Vessels of Dogs and Cats. J. H. Gaddum and P. Holtz.—p. 139.
Studies on Physiology of Reproduction: V. Suprarenal Cortex in Pregnancy and Lactation. Dorothy H. Andersen and Helen S. Kennedy.—p. 159.
Differential Pharmacology of Inferior Vena Cava of Some Mammals. K. J. Franklin.—p. 174.
Measurement of Red Cell Volume: IV. Alterations in Cell Volume in Hypotonic Plasma. J. Macleod and E. Ponder.—p. 181.
Investigation of Toxic Effects of Large Amounts of Sugar in Blood. C. Evans.—p. 189.
Rate of Blood Flow and Gaseous Metabolism of Uterus During Pregnancy. J. Barcroft, W. Herkel and S. Hill.—p. 194.

Medical Journal of Australia, Sydney

1: 1-42 (Jan. 7) 1933

Signs and Symptoms of Acute Stage of Anterior Poliomyelitis in 1931-1932 Epidemic. S. F. McDonald.—p. 1.
*Few Notes on Serum Treatment of Acute Anterior Poliomyelitis. A. E. Paterson.—p. 5.
*Discussion on Treatment of Anterior Poliomyelitis from Onset of Paralysis Till End of Spontaneous Recovery of Power in Muscles. L. W. N. Gibson.—p. 8.
Late Treatment of Anterior Poliomyelitis. A. V. Meehan.—p. 10.
Pathology of Acute Poliomyelitis. J. V. Duhig.—p. 14.
Epidemiology of Anterior Poliomyelitis, with Especial Reference to Queensland Epidemic, 1931-1932. J. G. Drew.—p. 26.

1: 43-74 (Jan. 14) 1933

Report of Epidemic of Poliomyelitis in New South Wales, 1931-1932. A. H. Tebbutt and K. Helms.—p. 43.
Recent Epidemic of Poliomyelitis from Physician's Point of View. E. H. M. Stephen.—p. 60.

Serum Treatment of Acute Anterior Poliomyelitis.—In an epidemic of acute anterior poliomyelitis, Paterson employed serum treatment in seventy-four patients, giving an average dose of 38.7 cc. During administration of the serum the patient was under an anesthetic and the dose, estimated

according to the time since onset, the child's general condition, and the cell count of the cerebrospinal fluid, was given: (1) at body temperature slowly through the lumbar puncture needle, already in situ, after 5 cc. more cerebrospinal fluid had been withdrawn; (2) intravenously by exposing a vein in the forearm. A further dose depended entirely on the child's progress and condition after twenty-four hours. The adoption of the intravenous route was the rule. The author concludes that, no matter to what extent paralysis is present, he is of the opinion that serum is beneficial as long as the patient is still febrile. The lives of some of his patients were saved by giving it, and in others it appeared to check further spread. In the future he aims to give larger doses, never to withhold serum even in the mildest of cases, to use combined intrathecal and intravenous administration and to produce a severe reaction.

Treatment of Anterior Poliomyelitis.—Gibson states that in the treatment of the late acute stages of poliomyelitis the essential factor is complete physiologic rest, mental as well as physical. Complete muscular rest is brought about by the fixation of the patients in plaster and splints. The patients are examined every day and their muscle groups are carefully and gently tested, and at the first sign of any muscular weakness fixation splints are applied immediately. The trunk and lower limbs are immobilized by the application of a complete plaster cast from the chest to the toes, the upper extremities by means of abduction splints of the birth palsy type. In the author's series of sixty-eight patients, the children were usually uncomfortable before the plaster cast was applied. In the convalescent stage, treatment consists of the immobilization of the patient's limbs and trunk in such a way that the weakened or paralyzed muscles are placed in a position of relaxation, and the institution of muscle training under the supervision of a skilled masseuse. The essential thing is not massage but muscle reeducation. Overdevelopment of the stronger muscles at the expense of the weaker ones should be avoided. When contractures occur, the weakened muscles are being continuously stretched and little recovery may be expected till the deformity is overcome. Early recognition of the disease and administration of the serum at a time when it is most efficacious will result in a favorable prognosis.

Practitioner, London

130: 113-232 (Feb.) 1933

Early Diagnosis of Malignant Disease. H. Waring.—p. 113.
Early Diagnosis of Malignant Disease of the Skin. J. M. H. MacLeod. —p. 120.
Early Diagnosis of Malignant Disease of Tongue. D. C. L. Fitzwilliams. —p. 134.
Early Diagnosis of Carcinoma of Stomach. T. I. Bennett.—p. 141.
Early Diagnosis of Malignant Disease of Throat. L. Colledge.—p. 151.
Early Diagnosis of Malignant Disease of Mediastinum, Lung and Pleura. L. S. T. Burrell.—p. 157.
Early Diagnosis of Malignant Disease of Colon. W. H. Ogilvie.—p. 163.
Early Diagnosis of Malignant Disease of Rectum. C. Gordon-Watson. —p. 172.
Early Diagnosis of Cancer of Breast. G. Keynes.—p. 181.
Early Diagnosis of Malignant Disease of Uterus. W. F. Shaw.—p. 189.
Early Diagnosis of Malignant Disease of Bone. E. P. Brockman.—p. 199.
Early Diagnosis of Malignant Disease of Bladder. A. E. Roche.—p. 206.
Early Diagnosis of Malignant Disease of Prostate. H. P. Winsbury-White.—p. 217.
Early Diagnosis of Malignant Disease of Testis. C. H. Carlton.—p. 225.

Tubercle, London

14: 145-192 (Jan.) 1933

Pulmonary Tuberculosis and Syphilis. O. Országh.—p. 145.
Tuberculous Bacillemia. J. Cribbin.—p. 163.

Japanese Journal of Experimental Medicine, Tokyo

10: 521-605 (Dec. 20) 1932

Experimental Research on Secretion of Stomach, Especially of Fundus Glands: IV. Mechanism of Secretion of Emulsion and Extract of Gastric Mucosa: Substance Stimulating Secretion of Gastric Mucosa. I. Sugishima.—p. 521.
Id.: V. Influence of Active Substance on Blood Pressure and Smooth Musculature. I. Sugishima.—p. 547.
Studies on Reaction of Complement Fixation with Vaccine Virus and Its Antiserum. G. Nakajima.—p. 559.
Experimental Studies on Time of Appearance of Postvaccinal Encephalitis. S. Ikei.—p. 563.
Studies on Virus of Smallpox. T. Taniguchi, M. Hosokawa, S. Kuga, Y. Komura and F. Nakamura.—p. 581.
Virus of Chickenpox. T. Taniguchi, M. Hosokawa, S. Kuga, F. Nakamura and S. Matsumoto.—p. 599.

Schweizerische medizinische Wochenschrift, Basel

63: 153-180 (Feb. 18) 1933

Distribution of Mortality from Cancer in Canton of Berne According to Districts and Its Different Localizations. G. Dardel.—p. 153.
*Treatment of Cancer of Lip. R. Stewart-Harrison.—p. 159.
*Tissue Stimulating Substance and Action of Massage. W. Ruhmann.—p. 163.
Problems in Carcinoma Therapy. A. Voegeli.—p. 165.

Treatment of Cancer of Lip.—On the basis of forty-two cases of cancer of the lip, Stewart-Harrison discusses the indications for and the results of the various therapeutic measures. He considers irradiation the method of choice for the treatment of the primary tumor usually consisting of pavement cells. In discussing the treatment of the regionary lymph nodes he recommends an expectant attitude as long as cancerous involvement is not suspected, but if they show signs of cancer he advises their removal by the Crile method, whenever this is possible, and he recommends postoperative roentgen irradiation, depending on the negative or positive histologic indications.

Tissue Stimulating Substance and Action of Massage.—According to Ruhmann, tissue stimulating substances (so-called tissue hormones) are constituent substances of the body that are liberated within the tissues by stimulation and increase the functional condition of these tissues or of their nervous and vascular apparatus, respectively. In comparing the effects of the iontophoretic introduction of the best known tissue stimulating substances (histamine, acetylcholine and the circulatory hormone of the pancreas) with those of massage, it was found that the iontophoresis with acetylcholine produced effects that resembled massage action most closely. From this the author concludes that the tissue stimulating substance liberated by massage is acetylcholine or is very closely related to it. Moreover, he believes that the hyperemia produced by massage in the deeper tissues is also the result of the liberation of cholinelike substances. Whereas acetocholine as such produces muscular contraction, it decreases the tension in the changed condition of the muscle during increased muscular tonus. The author thinks that the release of involuntarily increased muscular tension by massage is probably to be explained by humoral action. If the sympathetic nervous system conducts the pain, the decrease in pain conduction by massage may be the result of the liberation of a parasympathetically active tissue stimulant such as acetylcholine. It is probable that, in addition to cholinelike substances, other metabolic substances, such as adenosin, may play a part in the local action of massage, but it will require further studies to determine this.

Beiträge zur Klinik der Tuberkulose, Berlin

82: 1-132 (Jan. 16) 1933

Influence of Altitude on Tuberculous Guinea-Pigs That Have Been Sensitized Toward Light by Means of Eosin. L. Lange, Bamatter, Grüninger and Löwenstädt.—p. 1.
*Virulence Tests with Tubercle Bacilli. E. Butschowitz.—p. 66.
Relation Between Virulence of Tubercle Bacilli and Prognosis of Pulmonary Tuberculosis. O. Amrein.—p. 74.
*Pathogenesis of Acute Generalized Miliary Tuberculosis. I. Minguez. —p. 84.
Experimental Studies on Bone Tuberculosis. M. Mandelstamm.—p. 98.
Calcium and Therapy of Tuberculosis. T. Sternberg.—p. 122.
Instrument for Coagulation and Division of Pulmonary Adhesions in Pneumothorax by Means of High Frequency Current. G. Leendertz. —p. 128.

Virulence Tests with Tubercle Bacilli.—Butschowitz shows that former tests on the influence of the virulence of tubercle bacilli on the course of the disease were unsatisfactory, because they disregarded the agglomeration of the bacilli in the culture, and that, even if attempts are made to break up the colonies, agglomerations containing twenty bacilli and more still remain. He therefore concludes that pure cultures are not suitable for virulence tests, and he decided to use a material in which each bacillus was separate; namely, the tuberculous sputum. He counteracted the toughness and the semisolid condition of the sputum as well as the presence of other bacteria by treating the sputum with a dilute solution of sodium hydroxide, and thus he obtained a pure culture suspended in a neutral, weak hypertonic solution, in which all bacilli were separate. Another advantage of this method is that the bacilli have not undergone changes in virulence by different culture mediums. After the number of bacilli per cubic centimeter had been determined and the suspension had been diluted to the desired degree, 0.5 cc. was injected sub-

cutaneously into the inguinal region of guinea-pigs, and 0.01 cc. was transferred to Lubenau's egg culture mediums. The colonies were counted after five weeks and the inoculated guinea-pigs were carefully observed and killed after ten weeks. The author reaches the conclusion that there is no definite parallelism between the clinical picture and the virulence of the tubercle bacilli. In the seven cases observed by the author some relationship between virulence and course of the disease could be observed, but this influence was neither dominating nor regular. Other factors appear to play a more important part.

Pathogenesis of Acute Generalized Miliary Tuberculosis. — Minguez discusses the theories advanced by other investigators and describes his own observations on thirty-nine cases. He expresses the opinion that a tuberculous focus, in order to become the point of origin of an acute dissemination, has to contain numerous bacilli, its content must have become softened or even liquefied, and an erosion of the vascular wall must have taken place so that an open connection exists between the blood channels and the tuberculous focus with its liquefied and virulent content. Thus the blood stream can flush out the content of the tuberculous focus and disseminate it. A tabular report shows that in thirty-one of the thirty-nine cases the author was able to detect the focus of origin. He also found that the dissemination originates most frequently in the lymph nodes. In regard to the theories advanced by others, he states that the vascular tubercles described by Weigert are generally the result and not the cause of miliary tuberculosis, but he does not deny the possibility that occasionally a caseated tubercle of the vascular wall may become the focus of a miliary tuberculosis. He rejects the Liebermeister-Huebschmann theory as far as it refers to the pathogenesis of miliary tuberculosis, but he agrees with Loeschke that Buhl's foci are the points of origin for dissemination into the blood stream.

Deutsche Zeitschrift für Chirurgie, Berlin

238: 653-746 (Feb. 16) 1933

*Conservative and Operative Treatment of Pyloric Stenosis in Infants. O. Wiedhopf and H. Brühl.—p. 653.
*Experimental Studies of Treatment of Pancreatic Necrosis with Antitryptic Substances. J. Baumann.—p. 671.
Question of Influencing Bone Growth and Bone Regeneration. H. Boeminghaus.—p. 684.
Experiences with Klapp's Osteotomy. Bengen.—p. 705.
Clinical Value of Antistaphylolysin Reaction and of Staphylokinase Action. F. Mondry.—p. 713.
Experimental Studies in Prevention and Treatment of Fat Embolism. W. Rückert.—p. 730.
Clinical and Experimental Studies of Course of Freezing Process. C. Hempel.—p. 736.
Operation for Carcinoma of Lip. O. Wiedhopf.—p. 741.

Pyloric Stenosis in Infants.—Wiedhopf and Brühl report fifty-eight cases of pyloric stenosis in infants treated in the pediatric and surgical clinics of the University of Marburg from 1925 to 1932, in which 84 per cent of the patients were boys. No hereditary tendency was noted. Hypertrophy of the pyloric musculature was present in all the cases. Of the thirty-five patients treated conservatively, two died. The treatment consisted of frequent feedings of the smallest amounts of human milk, rectal infusions, subcutaneous administration of dextrose and Ringer's solution, and blood transfusions. Among the definite indications for conservative treatment the authors include a late onset, say at the end of the first three months of life, moderate vomiting and insignificant or no loss of weight. Intractable vomiting, rapid emaciation and the presence of complicating conditions constituted absolute indications for operative intervention. The authors emphasize that with the conservative method the convalescence is slow, requiring from two to four months of careful treatment before the normal state is reached. Roentgenologic studies revealed that atonic dilatation, absence of vigorous peristalsis, ptosis and delayed emptying of the stomach were present from two to five years later. The possibility of ptosis of adults having its origin in infancy is suggested. Of the fifteen operative cases, one was of a severe degree, eight were designated as intensely severe and five extreme. There were two fatalities. The recovery was remarkably smooth and the stomach assumed normal peristaltic vigor on the fourth postoperative day. The convalescence was much shorter than with the conservative method. Ramstedt's method of splitting the serosa and muscularis down to the mucosa was adopted.

Treatment of Pancreatic Necrosis with Antitryptic Substances.—Baumann demonstrated that the organism of a dog with experimental pancreatic necrosis is flooded with active trypsin, which is excreted in the urine of the animal in large amounts. The most advanced lesions were found in the kidneys and in the liver, corresponding to the localization of highest concentration of trypsin. The author in this work sought a substance capable of lowering the proteolytic action of trypsin. He found that acriflavine hydrochloride in a dilution of 1 : 15,000 reduced the capacity of trypsin to digest casein to one half and, in a dilution of 1 : 30,000, to one fourth. The author believes that irrigation of the peritoneal cavity with this substance in a case of acute hemorrhagic pancreatitis would have the effect of neutralizing the proteolytic activity of trypsin.

Medizinische Klinik, Berlin

29: 245-278 (Feb. 17) 1933

Fundus Oculi in Hypertension. R. Scheerer.—p. 245.
*Danger of Gangrene in Intermittent Claudication. H. Schlesinger.—p. 248.
Surgical Treatment of Severe Colitis. F. Mandl.—p. 251.
Resistance of Kidney Against Suppurative Infections. G. Wolfsohn.—p. 253.
*Parapulmonary Oxygen Administration as Therapy of Thyrotoxicosis. E. Flaum and O. Zimmermann.—p. 256.
Peculiar Pathogenesis of Case of Diabetes Mellitus. E. Kestermann.—p. 258.
Determination of Sugar Content of Urine. G. F. Materna.—p. 259.

Danger of Gangrene in Intermittent Claudication.—On the basis of 470 observations on 432 men and 38 women, Schlesinger concludes that intermittent claudication is rarely a symptom of anatomic changes in the arteries. He maintains that it is just as frequently a symptom of arteriosclerosis as of thrombo-angiitis obliterans, and he observed it most frequently in patients over 51 years of age. The danger of gangrene of the extremities is especially great in the first two years after the onset of the intermittent claudication. The patients with thrombo-angiitis are endangered to the end of the fifth year. In older patients the incidence of gangrene decreases after the third year, and in younger patients with the beginning of the sixth year. More than 8 per cent of all patients with intermittent claudication remain free from gangrene in spite of the fact that the intermittent claudication persists for many years. Patients who have intermittent claudication longer than six years (up to twenty years) rarely develop gangrene of a member; at least 83 per cent of this group remain free from gangrene. The most important etiologic factor is the abuse of nicotine, impairment by cold being much less important. The arterial disease causes periodic exacerbations and the intervening periods of improvement may last many years. This explains the relative benignity of many arterial disorders. Circumscribed gangrene does not indicate malignancy, for even repeated circumscribed gangrene may heal with shedding of the necrotic portions, and severe recurrence may be absent for years. Of forty patients, twelve were free from relapse and were able to work longer than six years after the first attack of gangrene. For this reason the author advises that crippling operations be postponed in the treatment of gangrene of the extremities and that conservative measures be tried.

Parapulmonary Oxygen Administration in Thyrotoxicosis.—Flaum and Zimmermann point out that Weinmann, when he employed oxygen in dental therapy, observed that the basal metabolism of his patients decreased as a result of the oxygen treatment. This observation and further studies by Weinmann and a collaborator induced the authors to try oxygen therapy in patients with thyrotoxicosis. The oxygen is applied to the gingiva under pressure of three atmospheres or more. As a result of the insufflation an emphysema develops, rapidly spreads and soon involves the mucous membrane of the lips and the surrounding subcutaneous tissues, so that a swelling of the lower eyelid and even of the forehead, chin and neck becomes noticeable. The emphysema generally persists for several hours. The authors repeated the treatment every day, each application lasting from two to fifteen minutes. In some patients only a few treatments were given, while in others they were continued for several weeks. Of the twenty patients with hyperthyroidism who were subjected to this treatment, seventeen were favorably influenced by the parapulmonary oxygen therapy. Not only did the increased metabolic rate decrease but the annoying heart palpitations disappeared. In a number

of cases the struma decreased, and in some cases even the exophthalmos receded somewhat. However, since in most instances the improvement was not lasting, the authors do not recommend this therapy as an independent intervention, but they think that whenever, for instance in intercurrent diseases, a temporary reduction in the metabolic rate is desirable, it can be employed with good success. They also suggest that it may replace the treatment with compound solution of iodine employed by many surgeons preparatory to strumectomy. It is superior to medication with compound solution of iodine in that it can be discontinued at any time without dangerous results, whereas in the course of the iodine treatment a temporary improvement is often followed by a considerable exacerbation necessitating an immediate surgical intervention. Moreover, there is a possibility that the favorable effects of the oxygen therapy may be lasting. The authors suggest that parapulmonary oxygen therapy may eventually prove helpful in combination with other conservative measures.

Münchener medizinische Wochenschrift, Munich

80: 245-286 (Feb. 17) 1933

*Tuberculosis of Small Children: Recognition and Treatment. H. von Mettenheim.—p. 245.
Dyskinesia of Biliary Passages (Cholepathia Spastica) and Surgery. V. Schmieden and H. Niessen.—p. 247.
*Nature and Treatment of So-Called Tennis Elbow. Hohmann.—p. 250.
Pathogenesis of Acute Pseudo-Uremia. E. Becher.—p. 252.
Treatment of Chronic Bacteriuria. O. Lürmann.—p. 255.
Determination of Vitamin C in Milk. B. Bleyer.—p. 257.
*Pollen Allergy. M. J. Gutmann.—p. 258.
*Pregnancy Toxicoses, Particularly Eclampsia and Its Preliminary Stages. L. Seitz.—p. 262.

Tuberculosis in Small Children.—Von Mettenheim states that the examination of nurslings and small children who are tuberculin positive has greatly improved in recent years by testing their gastric fluid on animals. This method has revealed that a much higher percentage of tuberculous children eliminate tubercle bacilli than was formerly believed. It showed that some of the so-called closed cases were "latent open." The author investigated the value of this method in sixty-eight children suspected of tuberculosis or found to be tuberculin positive. His observations corroborated the results of other investigators. The author discusses the significance of early recognition of tuberculosis and particularly the measures to be taken to prevent spreading of the infection. He emphasizes that the general practitioner should at least perform the percutaneous test in children suspected of having tuberculosis. Small children in institutions should be subjected to the skin test without exception. Children with a positive tuberculin reaction should be examined with roentgen rays, and these roentgenologic examinations should be repeated from time to time. Small children with pulmonary symptoms should be isolated and kept in institutions for better observation. In doubtful cases, animal experiments should be made with the gastric juice.

Tennis Elbow.—Hohmann considers the so-called tennis elbow an irritation of the periosteum developing as a result of overexertion of the extensors of the hand inserted on the lateral epicondyle of the humerus. Ordinary work taxes these muscles considerably, but exceptional exertion, such as is required in playing golf or tennis or in chopping wood, may cause changes not only in the overtaxed muscles but also at the site of attachment of these muscles in the richly innervated periosteum of the lateral epicondyle of the humerus. Traction on the periosteum irritates it and causes a typical periostitis, which may lead to the formation of deposits. In chronic cases the deposits may appear in the roentgenogram as fine seamlike thickenings or as cloudy or jagged formations. The diagnosis of epicondylitis is facilitated by Thomsen's manipulation, in which the closed fist of the patient is pressed against a resistance in the volar direction, while the elbow rests on a support. The pulling on the actively contracted dorsal flexors produces the typical pain at their site of origin, the epicondyle. The author points out that the brachioradialis muscle cannot have the significance in tennis elbow that many ascribe to it, and he differentiates typical epicondylitis from arthrosis of the radiohumeral joint. He recommends immobilization of the hand and elbow for the treatment of epicondylitis as long as the condition is still new, and he advises surgical intervention for chronic cases. Following anesthetization of the region of the epicondyle, he makes an incision 3 cm. long, across the anterior aspect of the epicondyle, and cuts into the fibers of the muscle tendon, releasing the tension by lengthening particularly the extensor carpi radialis brevis. This relieves the periosteal region on the epicondyle from the constant traction and gives it an opportunity to heal. The author considers unfounded the objection that this intervention might result in loss of power of the hand, provided only those fibers are divided which originate on the anterior protuberance of the epicondyle and in the adjoining slight depression. The epicondyle itself is usually free from changes, but, if the roentgenogram shows a spurlike exostosis, it should be removed. The flexed elbow is immobilized from eight to ten days by a plaster-of-paris cast. The favorable results of this operation obtained by the author in fifteen cases were corroborated by another author who employed it in four cases.

Pollen Allergy.—Gutmann discusses a few of the more important problems of hay fever and states that much is as yet unknown about its origin. The fact that pollen introduced into the nose of normal persons is eliminated unchanged, whereas in a hay fever patient sensitive to this particular type of pollen it is changed, some of it having burst, seems to indicate that either the mucous membrane or the mucus of the hay fever patient differs from that of a normal person. It may be that the allergic patient has an additional enzyme that breaks up the pollen, so that a toxin is liberated. After citing another test that indicates an increased dissolving power of the nasal secretion of the allergic patient, the author describes various attempts made to prevent the dissolving process or to counteract the influence of the dissolved substances, and he evaluates the various contributing causes. In discussing the clinical manifestations of pollen allergy, he emphasizes that it is a systemic disease with especial involvement of the eyes, nose, pharynx and bronchi, but that all other organs may become affected. Because he is convinced that it is a systemic disease, he advises the discontinuance of the term hay fever and the designation of the condition as pollinosis or pollen allergy. He points out that the general symptoms of pollinosis are not limited to fatigue and irritability but that there may be cutaneous manifestations in the form of herpes, urticaria or psoriasis, and that intestinal disorders, neuritic symptoms and urogenital and various other disturbances may develop in connection with pollen allergy. In discussing the diagnosis he evaluates the cutaneous reactions and expresses the opinion that tests with mixed extracts are not sufficient. He states that prophylactic treatment by desensitization is the most satisfactory therapy. In discussing the treatment during the hay fever season he tells of a patient who remained for hours in a meadow in spite of severe attacks of sneezing. Then blood was withdrawn from the cubital vein and 5 cc. of it was immediately injected intramuscularly. Three days later, 5 cc. of the serum was injected. This second injection was followed by severe local swelling but the patient remained free from hay fever symptoms for the remainder of the season. The author concludes with a discussion of the symptomatic treatment.

Toxicoses of Pregnancy.—Seitz points out that pregnancy effects considerable changes in the female organism and that in some women these changes lead to the manifestation of certain deficiencies. He mentions neurologic, dermatologic, hematologic and cholehepatic disturbances developing during pregnancy, but he gives especial consideration to eclampsia as characteristic of the later stages of pregnancy. He describes the clinical aspects of three different forms of eclampsia: the edematic-nephrogenic, the hepatogenic and the cerebral types. In discussing the therapy of eclampsia he points out that the recognition of its preliminary stages is of the greatest importance. During the last three months of pregnancy, edema should be watched for, the urine should be examined for the presence of albumin and casts, and the blood pressure should be taken regularly. The women should be asked about pressure pains in the right hypogastric region, visual disturbances, headaches, lack of appetite and nausea. Since in some pregnant women the capacity to decompose proteins and fats seems to be impaired, their diet should not contain too large quantities of these substances. On the other hand, carbohydrates are readily utilized; in fact, the pregnant organism is much more readily affected by a lack of carbohydrates than is the nonpregnant organism. Because of the tendency to the formation of edema and to nephropathic conditions, sodium chloride intake

has to be limited, but care should be taken that the pregnant woman receives adequate amounts of calcium, vitamins, iron and iodine. However, in spite of all precautions, eclampsia cannot always be prevented; if it does develop, conservative measures should be tried first.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

86: 595-863 (Feb. 7) 1933. Partial Index

Respiration of Erythrocytes in Anemia. K. Damblé.—p. 595.
Modification of Normal and Pathologic White Blood Picture by Roentgen Irradiation. E. Hayer.—p. 623.
*Influence of Sex Hormones on Creatine Metabolism. F. Bühler.—p. 638.
Form of Stimulation Process in Normal Heart Muscle Element. F. Schellong.—p. 659.
Iodine Metabolism. A. Sturm and R. Schneeberg.—p. 665.
*Various Causes of Distortion of Electrocardiogram and Their Elimination. W. Gaarz, G. Grosz and J. Rihl.—p. 675.
Changes in Alkali Reserve and in Sugar Content of Bile Under Influence of Various Physiologic Stimulants: Action of Histamine, Epinephrine and Insulin. W. M. Karatygin and A. I. Hefter.—p. 697.
Investigation on Uric Acid Metabolism in Experimental Disorders of Kidney. L. Kürti.—p. 709.
Can Curative Effects be Expected from Percutaneously Absorbed Water in Comparison to Physiologic Action of Perfolially Administered Water in Plants? E. Hiltner.—p. 716.
Fluctuations of Specific Hemolytic Power and of Chlorides of Blood Under Influence of Pain Stimuli. S. Balachowski and R. Messig.—p. 723.
Experimental Investigations on Organ Function Under Influence of Paravertebral Anesthesia. K. H. Erb and K. Thiel.—p. 728.
Significance of Reticulo-Endothelial System for Toxicity of Arsphenamines and Metal Colloids. A. Hasskó.—p. 759.
Technic of Suture of Vessel. T. Naegeli and F. Meythaler.—p. 769.
Elimination of Water by Respiration: Water Vapor Tension of Respiration Air in Diabetes Insipidus. A. von Czike.—p. 772.
Determination of Resistance of Erythrocytes Against Osmosis and Saponin. J. Kaulbersz.—p. 778.
Isolation of Group Specific Agglutinogens of Erythrocytes. A. Juhász-Schäffer and A. Vannoti.—p. 809.
Functional Testing of Kidney by Means of Dyestuffs for Glomeruli and Tubuli. L. Németh.—p. 817.
Influence of Anesthetics on White Blood Picture of Rabbits. G. Stier and B. Levy.—p. 822.
Synthesis of Gastric Function. F. Brauch.—p. 829.
Lipase Content of Lymph of Ductus Thoracicus. A. Kálló.—p. 848.
Influence of Liver Extracts on Vital Storage of Liver and Spleen. H. Bittersohl and K. Neidhardt.—p. 854.

Sex Hormones and Creatine Metabolism.—Bühler studied the creatine metabolism and the decomposition of creatine by hormones following intravenous injection of 500 mg. of creatine. His observations were made on persons in whom sexual function had ceased, on patients with incretory disturbances, on two patients with disorders of the muscles, and on children before puberty. The parenterally administered creatine was eliminated always unchanged in form but not always in quantity. Following hormone administration, but under otherwise unchanged conditions, a considerable decomposition of the creatine became manifest. However, in prepuberal children this action of the hormones was absent, for the children still eliminated the largest portion of the creatine. The male sex hormone influenced creatine decomposition only in men and the female sex hormone only in women. In the reverse condition the decomposition was inhibited. This proves that the action of the sex hormones on creatine exchange is sex specific. The author also describes a new method for the determination of the creatine-creatinine values in the urine. This method employs the step photometer of Pulfrich. The superiority of this method over other colorimetric tests is that it makes the use of a comparative solution unnecessary and that the reading, which is based on a standard curve, is simple.

Distortion of Electrocardiogram.—Gaarz and his collaborators show that the study of changes in the auricular and ventricular complexes, in order to detect myocardial disorders, demands a more exact reproduction of the impulse current than does merely an analysis of rhythmic disturbances. In view of the growing significance of electrocardiography it is important to recognize distortions that may appear in the electrocardiographic curve. The authors discuss the distortions that have their origin in the apparatus. Perhaps the most annoying distortions are those produced by strong current generators and conductors, particularly, if, as is now generally the case, the alternating current is used. The interference fields originating in them may become so disturbing as to make the operation of the electrocardiograph impossible. After showing that the interferences produced by a strong current unit in a nearby electrocardiograph may be of galvanic, electrical or magnetic nature, the authors discuss the means by which the disturbances can be eliminated, particularly the screening off of the electrocardiograph by metal protectors. Most of the disturbances caused by the patient are the result of muscular contractions that make the impulse current of the muscle appear in the electrocardiogram, or introduce currents into the electrocardiogram by causing displacements of the electrodes. In order to avoid distortions of this kind, care should be taken that the patient is completely at ease and relaxed. In many cases this will be sufficient but, if not, a sedative may be given some time before the test, or a discharging conductor must be employed. The author discusses the diagnostic errors that may be made if the distortions are not taken into consideration. For example, it may be difficult to decide whether there is a normal sinus rhythm in which the P deflection merely does not become clear, or whether an atrioventricular beat sequence is present in which the P deflections are masked by the QRS complex, or whether auricular fibrillation exists. In such cases the behavior of the rhythm may fail as a diagnostic aid, and the authors cite several other possibilities.

Zentralblatt für Gynäkologie, Leipzig

57: 497-544 (March 4) 1933

*Prevention of Puerperal Eclampsia. E. Waldstein.—p. 497.
Encephalomalacia in Eclampsia. K. Klaus.—p. 508.
Early Pregnancy Toxemia. P. Hussy.—p. 510.
Treatment of Vomiting of Pregnancy. E. Schafft.—p. 513.
Diabetes and Pregnancy. A. Eyding.—p. 514.
Conduct of First Stage of Labor. A. von Fekete.—p. 522.
Conduct of Labor in High Transverse Presentation. K. Burger.—p. 527.
*Method of Performing Legalized Abortion. S. Topuse.—p. 533.

Prevention of Puerperal Eclampsia.—In Waldstein's opinion, the incidence of puerperal eclampsia can be diminished by adoption of two measures: (1) artificial termination of pregnancy in patients with preeclamptic manifestations and (2) systematic examination of all women after delivery, paying particular attention to those manifesting preeclamptic symptoms and signs before and during delivery. The author found that patients with grave preeclamptic signs are less likely to develop puerperal eclampsia if delivered by operative means than the mild cases after spontaneous delivery. The beneficial effects of artificial delivery are due to the shortening of the time of labor and to the elimination of painful contractions, which tend to raise the blood pressure and to loss of blood. The author shares the view of Essen-Möller that preeclamptic signs exist before the delivery in all patients developing postpartum convulsions. To evaluate the efficacy of prophylactic measures, he presents two groups of patients. Group 1 comprises 21,474 women delivered between 1909 and 1927. No prophylactic measures were applied to the group. Group 2 comprises 10,737 patients delivered between 1927 and 1931, to whom the prophylactic measures were applied. In group 1 there were eleven cases of eclampsia developing during pregnancy, sixty-one at the time of delivery and forty-five in the puerperium, a total of 117 cases of eclampsia. In group 2 there were eight cases developing during pregnancy, fifteen at the time of delivery and five in the puerperium, a total of twenty-eight cases. Bearing in mind that the numerical relation between the two groups is as 2:1, it is seen that the number of eclampsias developing in the course of pregnancy but before delivery was greater in group 2 but that the number of eclampsias during delivery diminished by one half and the number of puerperal eclampsias was still smaller. The general incidence of eclampsia in the preprophylactic group was 1 in every 352 deliveries, in the prophylactic group 1 in 715. The incidence of puerperal eclampsia was 1 in 427 for group 1 and 1 in 2,147 for group 2. In group 2 there were five instances of puerperal eclampsia, an incidence of 0.46 per cent, as compared with that of 2.1 per cent of group 1. In discussing the influence of operative termination of labor and of spontaneous delivery on the development of puerperal eclampsia, the author points out that there were 471 patients in group 2 manifesting preeclamptic symptoms. Of these, 111 pregnancies were artificially terminated without development of puerperal eclampsia in a single instance. The five instances of puerperal eclampsia in this group took place after spontaneous delivery. Among the therapeutic measures adopted in the treatment of patients manifesting preeclamptic symptoms, the author emphasizes the salt free diet, and restriction of food and fluid intake to a point of starvation for the patients in a graver condition. Those in a mild con-

dition are allowed 0.5 liter of fluids daily in the form of fruit juices or tea, and carbohydrate food, preferably zwieback and fruit. Dehydration was accomplished by the use of diuretics, especially of theobromine and of thyroid preparations, and by the use of saline cathartics. The author advises against venesection on the ground that its effect is transient and that one cannot predict the amount of blood the patient will lose during delivery. Incisions into a rigid cervix, as advised by Scanzoni, were found of service in shortening the stage of cervical dilatation and making safe earlier application of forceps.

Method of Performing Legalized Abortion. — Topuse reports on 14,270 abortions performed in three hospitals of the city of Winnitza (Ukraine) from 1927 to 1931. It was noted that during the same period the number of spontaneous abortions diminished. The largest proportion of abortions, 88 per cent, were performed before the end of the third month of pregnancy. The author is opposed to all methods of abortion by induction of labor pains on the ground that any method which tends to keep the cervix open leads to infection. The author follows the method universally adopted in Russia of dilating the cervix with Hegar dilators and emptying the uterus. The injection of 10 cc. of 1 per cent solution of procaine hydrochloride into the posterior vaginal wall results in satisfactory anesthesia within ten minutes. The uterus is not packed. Patients are hospitalized for four days. There was not a death in 14,000 cases. A rise of temperature up to 38 C. (100.4 F.) occurred in 1 per cent of the cases. Four patients had higher temperature. Two of these developed a severe parametritis with subsequent abscess formation, one developed a unilateral adnexitis, while one developed a pelvic peritonitis of probable gonorrheal origin. All four patients recovered. Perforation, the most dreaded of all complications, occurred eight times, an incidence of 0.06 per cent. Termination of pregnancy advanced beyond three months was accomplished by vaginal cesarean section after the method of Dührssen, 145 such sections being performed without a fatality. The author concludes that, while the number of induced abortions was on the increase, the number of spontaneous abortions was on the decrease. The method of choice for patients under three months is operative dilation of the cervix and emptying of the uterine cavity at the same time.

Finska Läkaresällskapets Handlingar, Helsingfors

75: 1-101 (Jan.) 1933

*Notes on Achylia. O Mustelin.—p. 28.
Spondylolisthesis. G. Wallgren.—p. 40.
Remarks on Red Hot Iron and So-Called Bier's Cautery Together with Some Attempts with It. W. Sjöholm.—p. 56.

Achylia.—Mustelin says that of his 400 cases of achylia a scant third were caused by cancer of the stomach. Fully 10 per cent of the remaining cases were due to pernicious anemia, and a considerable number probably were caused by chronic gastritis. At least one fifth of all cases, not including those with cancer and pernicious anemia, are ascribed to a degenerative milieu and correspond to Martius' simple or constitutional gastric achylia.

Hospitalstidende, Copenhagen

76: 1-28 (Jan. 5) 1933

Intervertebral Disks: Review. H. Scheuermann.—p. 1.
Bulbocapnine Catalepsy. M. Ellermann.—p. 17.
*Fatal Pernicious Anemia Without Anemia: Case. T. E. H. Thaysen.—p. 23.

Pernicious Anemia Without Anemia. — Thaysen states that his case illustrates that the blood changes in pernicious anemia are only one link in the symptom complex of the disease and that liver treatment, even though it brings the hemoglobin percentage up to normal, does not protect against the development of a degeneration in the central nervous system which can cause death without the establishment of any localized cerebral disorder. Treatment with desiccated hog stomach in doses corresponding to 300 Gm. of fresh stomach had no effect on the symptoms of the central nervous system.

76: 57-84 (Jan. 19) 1933

Sterilizing of Surgical Instruments and the Like. L. E. Walbum.—p. 57.
*Age of Patients with Pernicious Anemia. S. A. Holbøll.—p. 72.
Meinicke Clarification Reaction in Syphilis. H. Boas and Elvira Øigaard.—p. 79.

Age of Patients with Pernicious Anemia.—Holbøll finds that essential pernicious anemia in Denmark occurs about twice as often in women as in men. The average age at the beginning of the disease is about 55 years for both sexes. In no more than 2 per cent of all cases does the disease manifest itself before the age of 30, and its occurrence in childhood is extremely doubtful.

Hygiea, Stockholm

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*Case of Actinomycosis of Pelvic Organs in Woman. G. Ahltorp.—p. 33.
Aschheim-Zondek's Pregnancy Reaction and Experiences with It. F. Settergren.—p. 45.

Actinomycosis of Pelvic Organs in Woman.—Ahltorp's case, probably salpingo-oophoritis and actinomycotic parametritis, objectively presented a pelvis resistance of varying size. After one and a half years' observation, fistulas broke through in the left gluteal region; actinomycotic granules were found in the pus. Roentgen and potassium iodide treatment and drainage of the gluteal abscesses resulted in a temporary improvement, followed by aggravation and death about seven months after the diagnosis of actinomycosis.

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Have Exogenous Factors in Pregnancy any Influence on State of Nutrition of the New-Born? K. U. Toverud.—p. 121.
Sedimentation Reaction in Pneumonia. K. Motzfeldt.—p. 141.
*Hepatogenic Diabetes. K. Motzfeldt.—p. 148.
*Rubeola-Encepalitis. K. Motzfeldt.—p. 153.
*Roentgenograms in Persons Rescued from Drowning. A. Klingenberg.—p. 156.
*Anaphylaxis After Wasp Stings. J. D. Arntzen.—p. 160.
Psychic Disturbances in Multiple Sclerosis. L. Melsom.—p. 165.
Trifocal Glasses for Cataract. S. Holth.—p. 168.
*Investigations on Liver Function in Mental Diseases, with Especial Regard to Relation Between Diseases of Liver, Enterogenic Intoxication and Undernutrition in Schizophrenia. A. Lingjærde.—p. 170.

Hepatogenic Diabetes.—Motzfeldt says that his patient with true, temporarily grave diabetes, probably had had a latent disorder rapidly aggravated by an infectious disturbance. Simultaneously with the diabetes a grave liver disorder was established. On regression of the diabetes the enlarged liver gradually decreased in size. The case was relatively insulin resistant. In the four years since treatment was administered, the patient, under constant control, has been well. In hepatogenic diabetes and other "paradiabetic" forms the possibility of recovery may be considered.

Rubeola-Encephalitis. — Motzfeldt's case of encephalitis after rubeola, believed to be the fifth reported, was characterized by the sudden onset of coma, hyperpyrexia and marked athetosis, four days after the appearance of the eruption. Death occurred after twenty-four hours. Necropsy revealed a generalized inflammation of the brain, especially of the white matter. The histologic picture closely resembled that in a case of encephalitis after measles previously reported by the author (*Norsk mag. f. lægevidensk.* **91**:481 [May] 1930).

Roentgenograms in Persons Rescued from Drowning. —Roentgenograms of the lungs of two patients, made thirty-four and seven hours, respectively, after their rescue from the point of drowning, showed dense diffuse shadows resembling infiltrations of the lungs and ascribed to atelectasis or possibly edema of the lungs. Klingenberg states that the shadows entirely disappeared after three and five days, respectively.

Anaphylaxis After Wasp Stings.—The four grave cases following a single wasp sting, of which two were fatal within an hour, described by Arntzen, are attributed to an abnormal hypersensitiveness to the proteins of the fluid injected by the sting, and not to the toxins.

Liver Function in Mental Diseases.—Lingjærde found that, in the active phase of schizophrenia, disturbances of the liver function are frequent, and necropsy not infrequently shows grave degenerative changes in apparently uncomplicated cases. Intestinal intoxication and malnutrition are considered causes. He concludes that the increased urobilinuria often noted in schizophrenia and other mental disorders is largely due to a carbohydrate deficiency in the diet and indicates increased administration of carbohydrates (and possible treatment with insulin). His investigations give no definite answer as to the possible rôle of liver disorders in the pathogenesis of schizophrenia.